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EDITORIAL

Mechanical Factors in Cardiac Rupture*

THE LIKELIHOOD of the occurrence of rupture of the ventricle subsequent to acute myocardial infarction is given in most reported series as between 1 and 10 per cent of the autopsy cases of myocardial infarction.[1–8] The past few years have witnessed an apparent increase in this incidence.[6–8] Some investigators have implicated the widespread use of anticoagulant therapy as a basis for this increase,[5–8] although it is important to differentiate between true rupture and hemopericardium secondary to pericardial irritation.

Early investigators stated that increased physical activity during the critical postinfarction period contributed to the etiology of rupture. Thus, Jetter and White in 1944 reported a higher incidence of rupture in patients in mental institutions than in patients in general hospitals, the inference being that the mental patients were more active.[9] Hypertension also was thought to be associated with a higher incidence of rupture.[10]

MECHANISMS OF RUPTURE

Two mechanisms have been implicated in the pathogenesis of rupture: (1) *elevation of intraluminal pressure*, whether produced by physical activity, by hypertension, or by valvular lesions; and (2) *dissection of the myocardium*, initiated perhaps by the unresolved stresses produced by contraction of the adjacent normal cardiac musculature.[11–13] Of course, it is possible that more than one mechanism may be involved.

Wessler, Zoll and Schlesinger pointed out that the pathologic substrate for rupture consists of a full thickness transmural infarction of the myocardial wall, and that the rupture usually occurs at the junction of the normal with the infarcted tissue, in areas lacking fibrosis or in recently infarcted areas.[14] Ruptures of the heart, when seen pathologically, are usually through the relatively thick portions of the ventricular walls, rarely through the thinner apex.[12] Ruptures are also rare in the thin walls of Rokitansky aneurysms unless a fresh infarction is also present in the area, or unless bacterial endocarditis is superimposed.[15] Typically, ruptures seen at autopsy are quite small and may be tortuous in their passage through the ventricular wall. A frequent site of endocardial tears is at the base of the papillary muscle, or in the area where the septum meets the free wall.[13]

CONTRIBUTING FACTORS

Several factors must be considered capable of contributing to myocardial rupture. First, infarcted muscle has different elastic properties than normal muscle. Also, as seen in Figure 1, healthy muscle during systolic contraction is pulling on the involved wall while at the same time, a paradoxical pulsation takes place in the infarcted area, with a systolic increase in the radius. This results, according to physical considerations (Law of LaPlace), in an increase in the radius and therefore of the tension in the wall. At the same time that the infarcted wall is stretched it tends to become thinner. Further, the stresses are concentrated at the junction of the normal and the infarcted muscle, predisposing to rupture at this point. It is at this junction that the fibers are twisted and bent during contraction and the paradoxical movement. Another factor acting in this area is that here there is a high concentration of leukocytes and proteolytic enzymes which may weaken the collagenous structure of the muscle wall. These forces all tend to focus the tendency to rupture at the junction of normal and infarcted tissue.

If the intraluminal pressure is increased there

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will be more ballooning of the weakened segment. If the diastolic volume increases there is a greater tension on the walls in both diastole and systole. This may be the contribution of hypertension toward rupture.

Fatigue Factor

It should be emphasized that the usual rupture complicating a myocardial infarction is not a blowout, such as might be produced by simple elevation of pressure. To illustrate this the following experiment was performed. Elastic

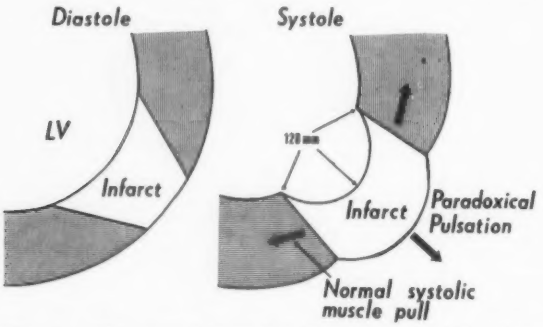

Fig. 1. Diagram of situation in transmural infarction. *Left*, in diastole there is no strain on the wall. *Right*, during systole the intact muscle pulls away from the infarcted area as indicated by the arrows. The infarcted wall is being stretched by paradoxical pulsation. The intraluminal pressure, the same for all points on the wall, causes increased tension in the infarcted portion since the radius of curvature is greater here. At the junctional area the fibers will be twisted and bent by the different forces acting upon them.

chambers, analogues of the heart, consisting of latex penrose tubing, were overdistended to the point of bursting by increasing the volume within them. These segments ruptured as a true blowout with the tear extending the entire length of the dilated segments and often being split off at the junction of the dilated and undilated segments in a T or H shape as in Figure 2. Other segments were filled and emptied in a pulsatile fashion by means of a pump. These ruptured after many hours of cycling, producing a small tear which was confined to only the dilated portion. The extent of rupture appears to depend on the tension in the wall at the time of rupture. When the latex tubing had been previously weakened by aging it in water, rupture occurred much earlier. Rupture took place at pressures and volumes which were lower than those the segment was able to withstand even in the immediately preceding cycle. If the speed of the pump was increased without changing the volume, rupture occurred earlier.

This problem is familiar to stress engineers who deal with problems of strength of materials. It is very similar to the problems of fatigue in metals. The static load that metals are able to bear is not the critical one, for in dynamic experiments rupture occurs at loads less than static.[16] This statistically predictable event is called "fatigue." Recently this concept has been extended to living tissues, and it has been pointed out that measurement of elastic static properties are of little value since other variables are operative in the dynamic state.[17] It is quite likely that twistings and compressions of the myocardial fibers, especially injured ones, will produce fracture of the fibers at less than the static load.

This type of fatigue apparently does not occur in normal hearts, since there are vital factors at work acting to repair any plastic deformation that might occur.

It has been pointed out that rupture occurs in areas involved by transmural infarcts. If there is an area of undamaged myocardial tissue present it appears to be sufficient to protect against rupture. Thomas was unable to produce rupture by injuring the epicardial surface of the left ventricle in rats by searing, and then subjecting the animals to exercise and respiratory obstruction in an effort to raise ventricular pressure.[18]

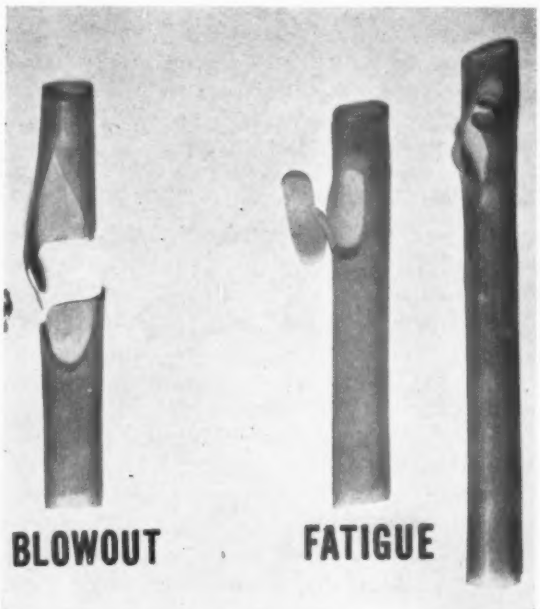

Fig. 2. *Left*, elastic tube ruptured by overdistention. The rupture is large and has completely severed the tube. *Right*, rupture in tubes caused by repeatedly filling and emptying them.

Clinical Implications

It seems likely that rupture of an infarcted muscle is a statistical accident, comparable to fatigue. The observed greater incidence in patients with hypertension or in those who have been physically active, may be caused not so much by an increase in intraluminal pressure as by the accompanying increase in heart rate; the dilatation of the heart with consequent increase in wall tension and resultant greater strength of muscular contraction; and the larger systolic radius of the paradoxically contracting infarcted area. Once a rupture is started, by whatever mechanism, it will be completed by the pull of the normally contracting muscle, and possibly by dissection from a jet of blood. An intramural hematoma, perhaps produced by anticoagulant therapy, may also be the source of this initial tear. This is extremely difficult to evaluate. It is unlikely that the presence of a mural thrombus can protect the heart against rupture.

Therapy of infarctions should be directed at minimizing stress in the myocardium. During the critical first week, avoidance of activity and anxiety with the concomitant results of tachycardia, pressure rise and increase in cardiac radius, may diminish the frequency of the occurrence of this complication. However, it must be recognized that even with the best regimen, this statistical accident is possible.

In summary, the pathogenesis of myocardial rupture in the course of infarction has been reviewed in the light of the mechanical situation. Paradoxical pulsation and normal systole combine to concentrate stress at the junction of the infarct with the normal tissue in the case of transmural lesions. "Fatigue fracture" of damaged fibers is more important than blowout.

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References

1. Askey, J. M. and Cherry, C. B. Rupture of the heart muscle in association with myocardial infarction. *Am. Pract. & Digest Treat.*, 1: 469, 1950.
2. Maher, J. F., Mallory, G. K. and Laurenz, G. A. Rupture of the heart after myocardial infarction. *New England J. Med.*, 255: 1, 1956.
3. Krumbhaar, C. B. and Crowell, C. Spontaneous rupture of heart: Clinicopathologic study based on 22 unpublished cases and 632 from literature. *Am. J. M. Sc.*, 170: 828, 1925.
4. Davenport, A. B. Spontaneous heart rupture; statistical summary. *Am. J. M. Sc.*, 176: 62, 1928.
5. Lee, K. T. and O'Neil, R. M. Anticoagulant therapy of acute myocardial infarction. *Am. J. Med.*, 21: 555, 1956.
6. Capeci, M. E. and Levy, R. L. The influence of anticoagulant therapy on the incidence of thromboembolism, hemorrhage, and cardiac rupture in acute myocardial infarction. *Am. J. Med.*, 26: 76, 1959.
7. Waldron, B. R., Fennell, R. H., Jr., Castleman, B. and Bland, E. F. Myocardial rupture and hemopericardium associated with anticoagulants. *New England J. Med.*, 251: 892, 1954.
8. Aarseth, S. and Lange, H. F. The influence of anticoagulant treatment on the occurrence of cardiac rupture and hemopericardium following heart infarction. *Am. Heart J.*, 56: 250, 1958.
9. Jetter, W. W. and White, P. D. Rupture of heart in patients in mental institutions. *Ann. Int. Med.*, 21: 783, 1944.
10. Edmondson, H. A. and Hoxie, H. J. Hypertension and cardiac rupture. *Am. Heart J.*, 24: 719, 1942.
11. Oblath, R. W., Levinson, D. C. and Griffith, G. C. Factors influencing rupture of the heart after myocardial infarction. *J. A. M. A.*, 149: 1276, 1952.
12. Segall, H. W. Rupture of ventricular myocardium. *Am. Heart J.*, 30: 39, 1945.
13. Beresford, E. H. and Earl, J. C. Spontaneous cardiac rupture. *Quart. J. Med.*, 24: 55, 1930–31.
14. Wessler, S., Zoll, P. M. and Schlessinger, M. J. Pathogenesis of spontaneous cardiac rupture. *Circulation*, 6: 334, 1952.
15. Askey, J. M. and Edwardes, A. F. Rupture of the heart muscle in association with coronary arterial disease. *Am. Pract. & Digest Treat.*, 1: 14, 1950.
16. Gumbel, E. J. Statistical interpretation of fatigue life and fatigue strengths. *Tr. New York Acad. Sc.*, 18: 334, 1956.
17. Remington, J. W. (ed.). Tissue Elasticity. Washington, D. C., 1957. Am. Physiol. Soc.
18. Thomas, W. C. Clinicopathologic and experimental observations on the pathogenesis of rupture of the heart due to myocardial damage. *Am. J. Path.*, 23: 904, 1947. (Abstr.)

Clinical Studies

The Effect of Sitosterol on Radioactive Fat Absorption Patterns*

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DURING the last several years various reports have appeared on the efficacy of certain plant sterols in lowering serum cholesterol levels. Although no definite explanation as to their mode of action is available, it has been postulated that they selectively block the absorption of ingested cholesterol.[1–3] The suggestion has also been made that these substances may interfere with absorption of fat and that this action contributes to their effectiveness in lowering the concentration of serum cholesterol.[4]

Recently, a test utilizing radioactive triolein has been found effective in revealing the fate of ingested fat.[5,6] Furthermore, this procedure has indicated that patients with coronary artery disease and/or hypercholesterolemia show a characteristic abnormality in their tolerance for fat.[7]

The purposes of this investigation were twofold: (1) to determine whether or not a plant sterol can influence fat absorption, and (2) to observe whether or not prolonged administration of this preparation may favorably affect an abnormal fat tolerance test.

MATERIAL AND METHODS

Acute Studies: Radioactive fat tolerance tests were performed on ten subjects according to the procedure previously described.[5] Five were normal control subjects and the remainder had severe coronary artery disease plus hypercholesterolemia (cholesterol level 350 mg. per cent and above). One week later, the procedure was repeated at which time 2 tablespoons (6 gm.) of sitosterol (cytellin-Lilly) were given immediately before the test dose of radiotriolein.

Chronic Studies: Ten additional patients with coronary artery disease and elevated cholesterol levels who had previously shown abnormal

TABLE I

Radioactive Fat Absorption Values With and Without the Administration of Cytellin in Normal Subjects and in Patients With Coronary Artery Disease

Case No.	Procedure	Whole Blood Radioactivity Levels (% of ingested fat) (hours after test meal)					
		4	6	8	10	12	24
	Normal Subjects						
1	RAF	5.7	9.2	5.8			2.2
	RAF + CYT.	8.6	8.9	7.4			2.1
2	RAF	7.2	11.2	10.8			2.0
	RAF + CYT.	6.8	10.4	12.0			2.2
3	RAF	6.4	9.1	10.2			1.8
	RAF + CYT.	5.6	8.2	11.6			2.4
4	RAF	8.2	11.6	9.1			2.0
	RAF + CYT.	9.0	12.0	12.6			2.6
5	RAF	5.1	12.2	10.0			1.6
	RAF + CYT.	4.2	6.8	9.1	12.8		4.0
	Patients with Coronary Disease						
6	RAF	4.2	11.1		22.2	18.7	13.5
	RAF + CYT.	8.1	11.4		20.0	18.7	13.6
7	RAF	6.7	10.4	10.4	16.0		7.6
	RAF + CYT.	15.8	24.6	20.0	18.2		11.0
8	RAF	5.0	12.8	12.0	17.4		6.5
	RAF + CYT.	9.4	17.7	17.0	19.0		8.1
9	RAF	3.4	10.4	11.0	16.8		5.8
	RAF + CYT.	15.0	25.0	20.0	19.2		8.6
10	RAF	14.7	12.0	16.8	20.0		11.5
	RAF + CYT.	7.4	7.4	17.0	23.3		18.5

NOTE: RAF = radioactive fat; CYT. = cytellin.

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tolerance to ingested radioactive fat were treated over a four to six month period with daily administration of 9 gm. of cytellin in divided doses just prior to each meal. The diet was essentially normal with no fat restriction.

Duplicate serial cholesterol determinations were made at monthly intervals in the fasting state. At the end of the test period the radioactive fat tolerance test was again performed.

Results

Studies Without Sitosterol: The initial radioactive triolein study in each of the five normal subjects conformed to the pattern we have previously described[6,7] (Table I). Thus, at the peak value, the whole blood radioactivity level was less than 15 per cent and the lipid value was less than 5 per cent. At the 24-hour interval, whole blood activity was less than 5 per cent and lipid blood contained less than 0.5 per cent.

Absorptive patterns in the patients with coronary disease (Table I) showed elevated whole blood and lipid blood radioactivity levels at both the peak and 24-hour time.

Sitosterol Studies: In none of the patients studied was there any apparent effect on the absorption of the radioactive fat by the prior administration of the cytellin (Table I, Fig. 1). Actually, in five patients, the blood levels obtained were higher in those cases in which the sitosterol was given. Using the same dose of cytellin but decreasing the amount of fat in the test meal by half likewise produced no

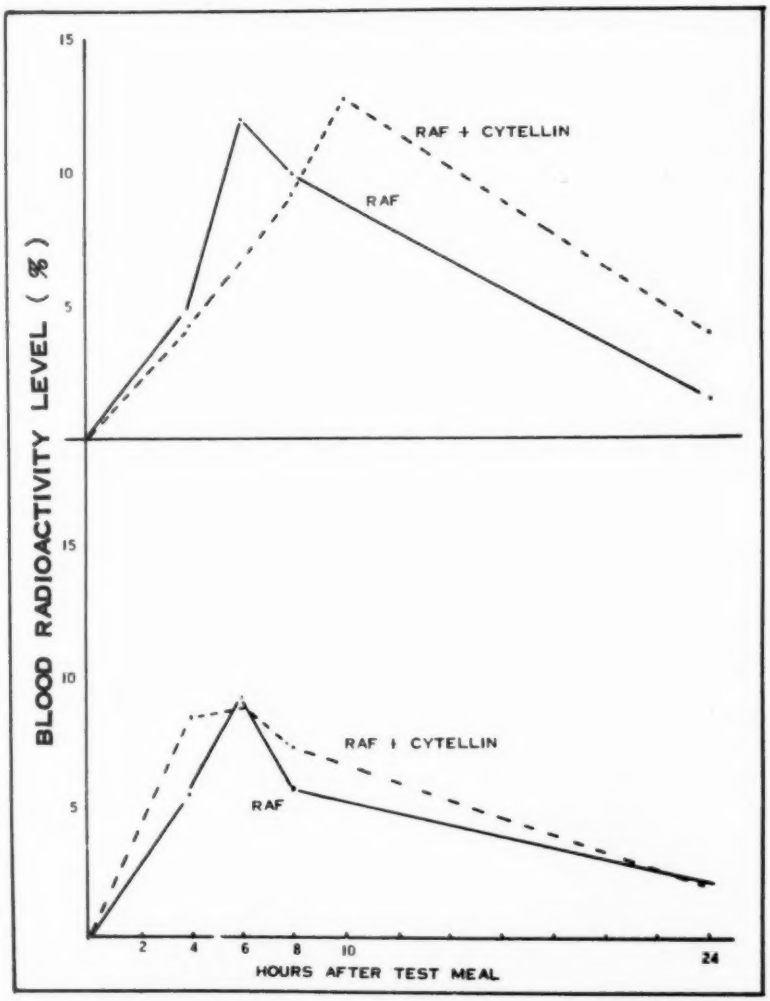

Fig. 1. Radioactive triolein blood levels with and without simultaneous administration of cytellin in normal subjects (*upper*, Case 5, *lower*, Case 1, Table I).

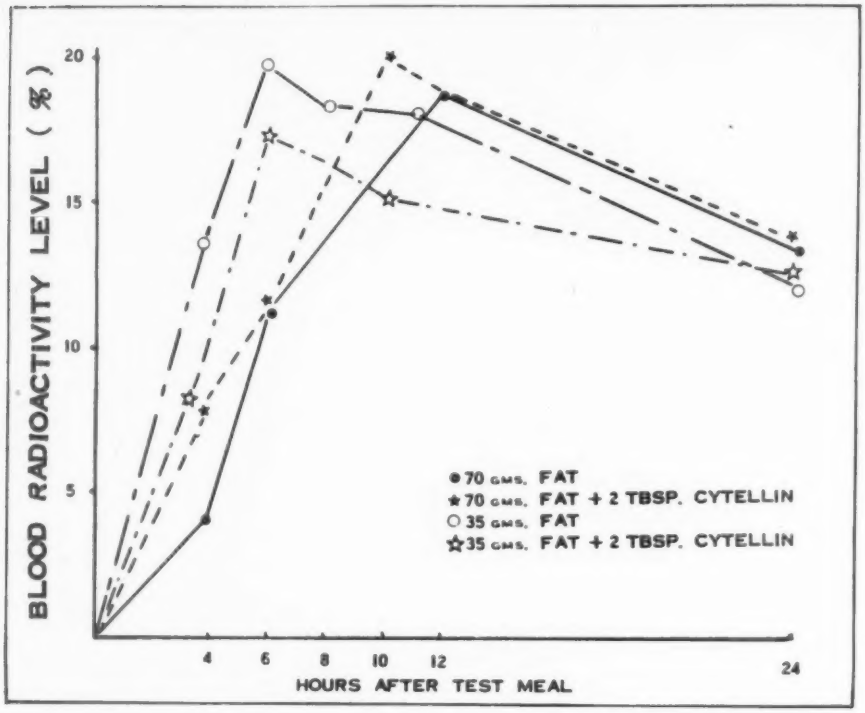

FIG. 2. Radioactive triolein blood levels with and without simultaneous administration of cytellin in patient with coronary artery disease and hypercholesterolemia (Case 6, Table I).

change in the blood absorption pattern (Fig. 2).

Prolonged administration of the cytellin to ten patients with coronary artery disease and hypercholesterolemia was ineffectual in lowering the blood cholesterol level except in one case (Table II).

Radioactive fat tolerance tests performed at the end of the treatment period showed no appreciable changes from the pretreatment values, even in the one case in which the cholesterol level had become normal (Fig. 3, lower half).

TABLE II

Changes in Blood Cholesterol Levels During Prolonged Administration of Cytellin in Patients with Coronary Artery Disease and Hypercholesterolemia

Case No.	Age (yr.), and Sex	Cholesterol Level (mg. %)								% Variation from Initial Level
		Before Treatment	(Months of Treatment)						Mean Level During Treatment	
			1	2	3	4	5	6		
11	48, F	349	320	278	308	340	285	310	307	−10
12	39, M	365	400	391	375	406	318	340	371	+ 2
13	42, M	320	287	310	325	295	280	310	302	− 6
14	45, M	439	380	310	440	510	380	370	398	− 9
15	50, F	309	390	370	310	320	350	400	357	+16
16	60, F	304	276	273	470	368	302	350	340	+12
17	38, M	350	420	520	400	375	370	345	405	+16
18	50, M	310	300	290	270	300	290	310	293	− 6
19	61, F	455	476	450	400	390	370	450	422	− 7
20	40, M	362	286	332	263	280	280	210	275	−24

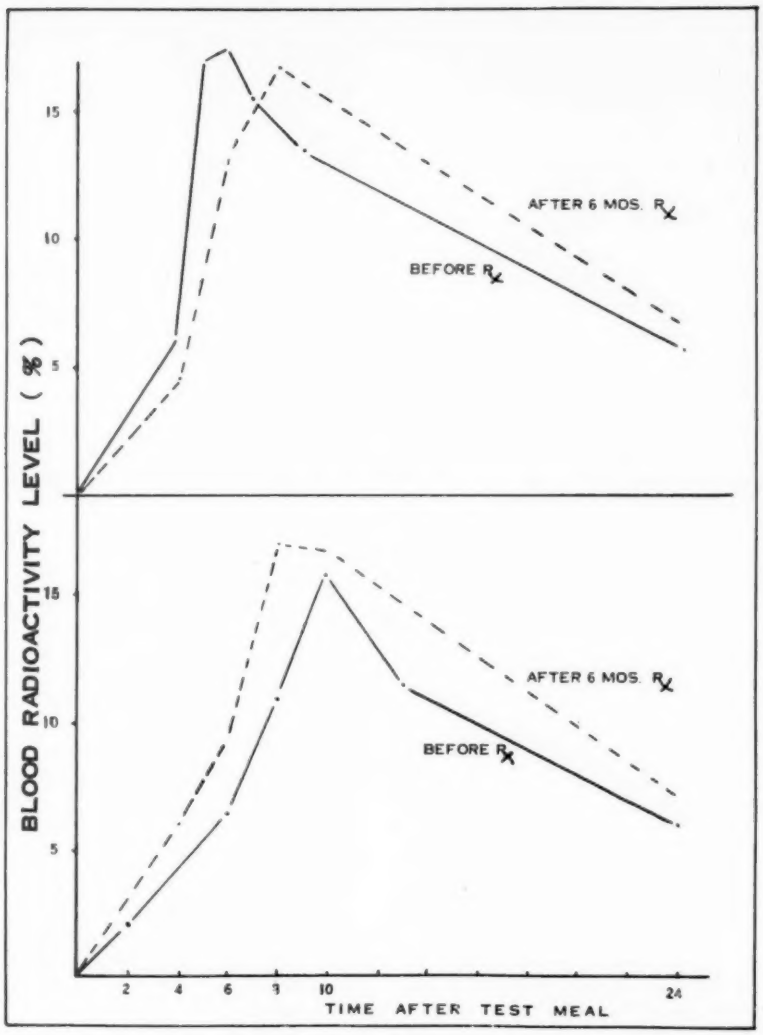

FIG. 3. Radioactive triolein absorption patterns before and after prolonged treatment with cytellin in patients with coronary atherosclerosis and elevated blood cholesterol values (*upper*, Case 13, *lower*, Case 20, Table II).

COMMENTS

The present studies indicate that sitosterol does not decrease neutral fat absorption when given immediately prior to a fat meal. Actually in a number of cases, the blood radioactivity levels were higher after the administration of cytellin than before. Although the reason for this is not altogether clear, it has been shown that as much as 10 per cent of ingested sitosterol may be absorbed.[8,9] If this occurred in our subjects, the resultant increase in the circulating fat pool could have produced elevated radioactive fat levels by a dilution effect.

Prolonged treatment with cytellin in patients with coronary artery disease and hypercholesterolemia did not significantly alter the blood cholesterol levels except in one patient. This has also been the experience of Driesbach[10] and Wilkinson[11–13] whereas others have found this therapy to be of definite value.[3,4,14–18] The recent critical studies dealing with the spontaneously occurring fluctuations in serum cholesterol values, however, make it mandatory to reappraise these data.[13,19]

Of more significance is the fact that in no case was there any improvement noted in the patient's intolerance to fat even in that individual in whom the serum cholesterol fell while undergoing treatment. Other studies, currently in progress, in which various mixtures

of unsaturated fatty acids are being used in an attempt to lower cholesterol levels, have likewise indicated that success in this regard is not reflected by an improved fat tolerance. This suggests that cholesterol levels alone are incomplete guides in the treatment of errors in fat metabolism.

Summary

1. Concomitant administration of a plant sterol (cytellin) with radioactive triolein did not decrease the absorption of the tagged fat.

2. In a group of patients with coronary artery disease and hypercholesterolemia prolonged treatment with this preparation produced no appreciable change in their radioactive fat tolerance even when the serum cholesterol level decreased to normal.

3. Reliance on blood cholesterol levels alone is probably an incomplete guide as to the effectiveness of "antiatherogenic" medication.

Acknowledgment

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References

1. Peterson, D. W. Effect of soybean sterols in the diet on plasma and liver cholesterol in chicks. *Proc. Soc. Exper. Biol. & Med.*, 78: 143, 1951.
2. Hernandez, H. H., Peterson, D. W., Chaikoff, I. L. and Dauben, W. G. Absorption of cholesterol-4-C^{14} in rats fed mixed soybean sterols and beta sitosterol. *Proc. Soc. Exper. Biol. & Med.*, 83: 498, 1953.
3. Best, M. M. and Duncan, C. H. Modification of abnormal serum lipid patterns in atherosclerosis by administration of sitosterol. *Ann. Int. Med.*, 45: 614, 1956.
4. Best, M. M., Duncan, C. H., Van Loon, E. J. and Wathen, J. D. The effects of sitosterol on serum lipids. *Am. J. Med.*, 18: 61, 1955.
5. Berkowitz, D. and Sklaroff, D. The use of radioactive fat in the study of absorption in various disease states. *Arch. Int. Med.*, 100: 951, 1957.
6. Berkowitz, D., Sklaroff, D., Woldow, A., Jacobs, A. G. and Likoff, W. Blood absorptive patterns of isotopically-labeled fat and fatty acid. *Ann. Int. Med.*, 50: 247, 1959.
7. Likoff, W., Berkowitz, D., Woldow, A., Jacobs, A. G., and Sklaroff, D. M. Radioactive fat absorptive patterns: their significance in coronary artery atherosclerosis. *Circulation*, 18: 1118, 1958.
8. Gould, R. G. Absorbability of beta-sitosterol. *Tr. N. Y. Acad. Sc.*, 18: 129, 1955.
9. Ivy, A. C., Lin, T. M. and Karvinen, E. Absorption of dihydrocholesterol and soya sterols by the rat's intestine. *Am. J. Physiol.*, 183: 79, 1955.
10. Driesbach, R. H., Brown, B., Myers, R. B. and Cutting, W. C. Effect of soy sterols on cholesterol atherosclerosis in rabbits. *Fed. Proc.*, 12: 317, 1953.
11. Wilkinson, C. F., Jr., Boyle, E., Jackson, R. S. and Benjamin, M. R. Effect of varying the intake of dietary fat and the ingestion of sitosterol on lipid and lipoprotein fractions of human serum. *Metabolism*, 4: 302, 1955.
12. Wilkinson, C. F., Jr. Effect of lipotropes and sitosterol on the level of blood lipids and the clinical course of angina pectoris. *J. Am. Geriatrics Soc.*, 3: 381, 1955.
13. Levere, A. H., Bozian, R. C., Craft, G., Jackson, R. S. and Wilkinson, C. F., Jr. The "sitosterols:" variability of serum cholesterol levels and difficulty of evaluating decholesterolizing agents. *Metabolism*, 7: 338, 1958.
14. Pollak, O. J. Reduction of blood cholesterol in man. *Circulation*, 7: 702, 1953.
15. Joyner, C. R. and Kuo, P. T. The serum cholesterol level and lipoprotein pattern following the administration of plant sterols. *Circulation*, 10: 589, 1954.
16. Barber, J. M. and Grant, A. P. The serum cholesterol and other lipids after administration of sitosterol. *Brit. Heart J.*, 17: 296, 1955.
17. Sachs, B. A. and Weston, R. E. Sitosterol administration in normal and hypercholesterolemic subjects. *Arch. Int. Med.*, 97: 738, 1956.
18. Farquhar, J. W., Smith, R. E. and Dempsey, M. E. The effect of beta sitosterol on the serum lipids of young men with arteriosclerotic heart disease. *Circulation*, 14: 77, 1956.
19. Rivin, A. U., Yoshino, J., Shickman, M. and Schjeide, O. A. Serum cholesterol measurement—hazards in clinical interpretation. *J. A. M. A.*, 166: 2108, 1958.

The Effect of Calcium Chelation on Cardiac Arrhythmias and Conduction Disturbances*

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THE SYNERGISTIC EFFECT exerted by calcium on digitalis activity has been recognized for many years.[1-3] Calcium ion concentration greatly influences the systolic action of digitoxin on frog hearts, and the positive inotropic effect of digitalis is dependent on the presence of calcium. Whereas the action of digitalis may in part be due to its effect on the regulation of potassium concentration within myocardial cells, calcium probably further influences cellular permeability of the myocardium to potassium ions.[4-8] Both digitalis and calcium are believed to increase myocardial irritability by promoting the outflow of intracellular potassium from myocardial muscle. Calcium, even in the absence of digitalis, may affect cardiac function in a manner somewhat similar to that of digitalis.[9]

The synergism between calcium and digitalis has also been demonstrated in the presence of digitalis intoxication.[2,10,11] The production of ventricular premature contractions and ventricular fibrillation in dogs by the administration of toxic doses of ouabain is enhanced by induced hypercalcemia. In man, the rapid administration of calcium to digitalized patients has been associated with fatal results.[12] Recently a "calcium-digitalis tolerance test" was proposed in which calcium is administered to digitalized patients, the end point occurring at the time when digitalis intoxication is produced by the added calcium.[11]

Recent reports have indicated that the induction of hypocalcemia will eradicate cardiac arrhythmias due to digitalis intoxication.[7,10,13] Page and Real[10] have demonstrated the reversal of digitalis intoxication in dogs by lowering the serum calcium with sodium versenate (NaEDTA), and subsequent clinical reports have verified the salutory effects of calcium chelation on digitalis intoxication in man.

NaEDTA† is a chelating agent which binds the serum calcium and effects a transient hypocalcemia when given intravenously.[14] Bechtel et al.[15] have demonstrated that 3 gm. of NaEDTA can be safely administered intravenously during a thirty-minute period, although some minor side effects such as tingling of the lips may occur. Gubner and Kallman[13] have reported the reversal of digitalis intoxication in several cases using 600 mg. of NaEDTA; greater amounts have been used by others.[16] Renal toxicity and coagulation disturbances have been reported following the use of NaEDTA, but only with much larger doses (200 to 440 mg./kg. of body weight) and with prolonged administration for eight to eleven days.[17]

The present study was undertaken to determine the effect of calcium chelation with NaEDTA on arrhythmias and conduction disturbances occurring with and without digitalis intoxication.

METHOD OF STUDY

Twenty-seven clinical trials with NaEDTA were performed on patients at the Jewish Hospital of St. Louis. Initially a standard 12-lead electrocardiogram was recorded. Before starting the infusion of NaEDTA, a three-minute continuous electrocardiogram was recorded for control purposes. The infusion consisted of 3 gm. of NaEDTA mixed with 400 cc. of 5 per cent glucose in water. The mixture was rapidly given intravenously, so that the entire infusion usually lasted about thirty minutes. Electrocardiographic tracings, consisting of at least 100 consecutive beats, were taken at 5-

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† Sodium versenate was generously supplied by Riker Laboratories, Los Angeles, California.

TABLE I
Effect of NaEDTA Therapy

Case No.	Abnormal Rhythm or Conduction Disturbance	Effect of EDTA Therapy	Onset of Effect After Start of Infusion	Duration of Effect	Serum Calcium (mg. per 100 ml.)		Serum Potassium (mg. per 100 ml.)	
					Before	After	Before	After
Group A: Patients with Digitalis Intoxication								
1 (A. G.)	Ventricular premature contractions	95% reduction in number of ventricular premature contractions	20 min.	2 hours	8.5	6.64	—	—
2 (E. V.)	Ventricular premature contractions	93% reduction in number of ventricular premature contractions	23 min.	75 min.	9.6	8.5	3.94	3.14
3 (A. H.)	Ventricular premature contractions	82% reduction in number of ventricular premature contractions	25 min.	15 min.	9.2	8.8	4.9	4.9
4 (G. H.)	Prolonged P-R (0.22–0.24 sec.)	Change of contour of P wave; P-R interval decreased to 0.16–0.20 sec.	20 min.	25 min.	—	—	—	—
5 (I. C.)	Prolonged P-R (0.30 sec.) and runs of Wenckebach conduction	P-R interval decreased to 0.22–0.24 sec.	30–35 min.	60 min.	9.9	7.5	3.32	2.38
6 (D. D.)	Atrial tachycardia with Wenckebach conduction	Atrial rate first slowed and block diminished; sinus rhythm then appeared	Initial change at 5 min.; sinus rhythm appeared at 30 min.	10–15 min.; atrial rate then increased	9.4	6.26	3.52	3.14
7 (D. K.)	Atrial tachycardia with varying block	Sinus rhythm appeared during infusion	20 min.	Permanent	—	—	—	—
8 (A. M.)	Runs of atrial tachycardia with block and sinus rhythm with blocked atrial premature contractions	Sinus rhythm without atrial premature contractions present at end of infusion	30 min.	15 min.	9.0	6.7	3.4	2.9
9 (S. S.)	A-V dissociation; atrial rate 53; ventricular rate 65	Atrial rate slowed to 32, ventricular rate slowed to 45	10 min.	60 min.	9.4	7.5	3.4	3.3
10 (M. Z.)	Bidirectional tachycardia	Reverted to atrial fibrillation	7 min.	Permanent	8.1	7.2	4.04	3.72
11 (I. P.)	Double tachycardia; atrial rate 120: nodal rate 80	Sinus rhythm with interval P-R appeared	10 min.	?	—	—	—	—

minute intervals during the infusion and for the first fifteen minutes thereafter. Follow-up electrocardiograms were subsequently obtained as indicated.

Prior to the start of the infusion, blood samples were drawn for determination of serum calcium and phosphorus levels. (During the earlier trials, serum potassium, sodium, chloride and carbon dioxide were also determined but this was abandoned when it was found that there were no consistent changes in the concentrations of these substances.) At the end of the infusion, blood was drawn from the opposite arm for serum calcium and phosphorus determinations. In several instances, as noted in Table I, these determinations were not carried out.

Each patient was carefully evaluated clinically for evidence of digitalis intoxication. In most cases, the presence or absence of digitalis

Table I (*Continued*)

Group B: Patients without Digitalis Intoxication

12 (C. H.)	Atrial fibrillation (AF) with ventricular premature contractions	No change	—	—	10.8	8.15	2.87	2.54
13a (M. M.)	Quadrigeminy due to ventricular premature contractions	All ventricular premature contractions disappeared	5–10 min.	3 hours	9.4	7.2	3.4	2.54
13b (M. M.)	Bigeminy and quadrigeminy due to ventricular premature contractions	Ventricular premature contractions intermittently disappeared	36 min.	60 min.	9.2	6.2	3.94	3.42
14 (F. B.)	Ventricular premature contractions	No change	—	—	9.7	7.65	4.04	3.42
15 (G. H.)	Atrial and ventricular premature contractions	No change	—	—	9.8	8.5	2.96	2.62
16 (A. S.)	Ventricular premature contractions	No change	—	—	9.7	7.5	4.28	3.94
17 (C. B.)	Ventricular premature contractions	No change	—	—	8.3	7.35	2.7	2.54
18 (F. S.)	P-R interval 0.26 sec.	No change	—	—	10.2	7.8	3.83	3.04
19 (C. W.)	P-R interval 0.22–0.24 sec.	No change	—	—	8.9	6.8	3.94	3.42
20 (C. P.)	P-R interval 0.23 sec.	No change	—	—	9.4	7.85	—	—
21 (C. D.)	P-R interval 0.26 sec.	No change	—	—	10.8	7.8	6.3	2.7
22 (G. S.)	P-R interval 0.28 sec.	No change	—	—	8.7	7.2	3.7	3.4
23 (W. A.)	Atrial tachycardia with block	No change	—	—	12.7	7.5	2.46	2.15
24 (J. A.)	Mixed rhythm; atrial fibrillation, atrial flutter and sinus rhythm with atrial premature contractions	No change	—	—	7.8	6.6	2.62	2.23

intoxication was established to our satisfaction, although in many instances this could only be determined after many days of careful observation. Of the twenty-seven trials, eleven were performed in patients with digitalis intoxication, while fourteen were carried out in patients considered to be free of digitalis intoxication. In two instances, the presence or absence of digitalis intoxication could not be satisfactorily established.

Results

The results of the NaEDTA infusions are tabulated in Table I.

Group A: Patients with Digitalis Intoxication (Table I): Frequent ventricular premature contractions occurred in three patients in this group. In each instance a substantial reduction in the number of ventricular premature contractions occurred following treatment with NaEDTA. The duration of effect of the drug in these cases was from fifteen minutes to two hours.

Impaired A-V conduction was present in two cases. In both instances a significant change occurred following the infusion of NaEDTA. Wenckebach conduction, which was present in Case 5, disappeared and the P-R interval was

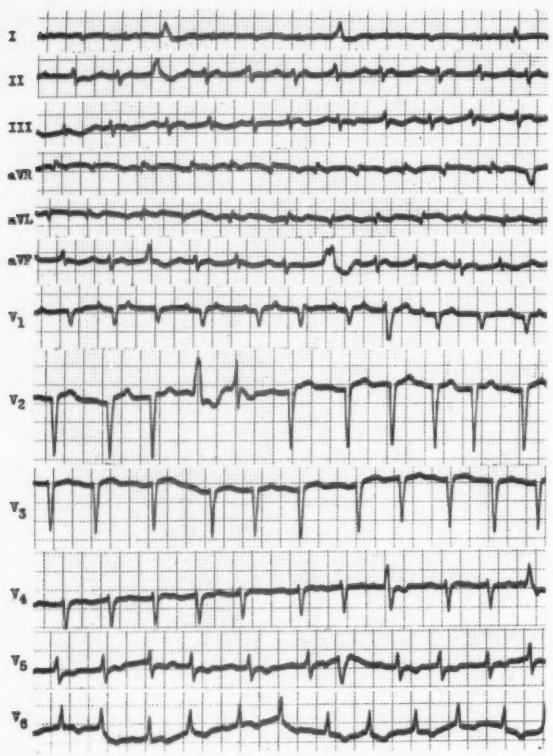

FIG. 1. Case 6 (D. D.). Atrial tachycardia with A-V block immediately before treatment with NaEDTA.

reduced to 0.22 to 0.24 second. The P-R interval did not drop below this level despite cessation of digitalis therapy. The effect of NaEDTA therapy was transitory, lasting twenty-five minutes in one case and sixty minutes in the other.

Atrial tachycardia with block was present in three cases. In Case 8, long periods of sinus rhythm with blocked atrial premature contractions were also noted. In Case 6, the atrial rate slowed in a gradual manner before sinus rhythm appeared (Figs. 1 and 2). In Case 7, sinus rhythm appeared abruptly without previous slowing of the atrial rate. In Case 8, the atrial premature contractions suddenly disappeared. Although the effect of NaEDTA therapy lasted only fifteen minutes in Cases 6 and 8, the arrhythmia was permanently abolished in Case 7.

One case of A-V dissociation was investigated (Case 9). Both the atrial and ventricular rates were slowed considerably with NaEDTA therapy, but A-V dissociation remained as the basic rhythm.

One case of bidirectional tachycardia (Case 10, Fig. 3) and one of simultaneous atrial and nodal tachycardia (Case 11) were studied. In both instances, the arrhythmia was rapidly terminated by the infusion of NaEDTA.

Group B: Patients without Digitalis Intoxication (Table I): Ventricular premature contractions were present in seven instances. In Case 13, the patient recieved NaEDTA on two occasions and the ventricular premature contractions disappeared both times, despite the fact that the patient had received no digitalis. In the remaining five trials, no effect on the number of ventricular premature contractions was noted. However, the hypocalcemia was of similar magnitude in all cases.

In five patients with prolonged P-R intervals, no change in A-V conduction was induced by the administration of NaEDTA.

In one case of atrial tachycardia with block (Case 23) and in one case of intermittent atrial fibrillation, flutter and tachycardia (Case 24) there was no change following infusions of Na-EDTA.

The presence or absence of digitalis intoxication could not be definitely determined in two cases, which are not tabulated. In one instance, atrial tachycardia with block was present. The P-R interval was prolonged in the other case. No effect was noted after the administration of NaEDTA in either case.

The changes occurring in the serum calcium and phosphorus levels with the infusions of NaEDTA are listed in Table I. In each case in which measurements were made, there was a definite fall in serum calcium associated with a drop in the serum phosphorus. The fall in serum calcium varied from 0.4 mg./100 cc. to 2.5 mg./100 cc.

In general, the infusions were well tolerated. Usually, the patients complained of mild aching in the arm and shoulder on the side in which the infusion was being given. The ache was diminished by the application of a hot water bottle. Occasionally some tingling of the lips occurred. These symptoms disappeared almost immediately following the termination of the infusion, in every instance.

COMMENTS

In each case of digitalis intoxication, a pronounced effect of the NaEDTA was produced. In one patient, however, the underlying rhythm, which was A-V dissociation, remained while the atrial and ventricular rates were both markedly slowed. The initial changes began as early as five to ten minutes after the start of the infusion

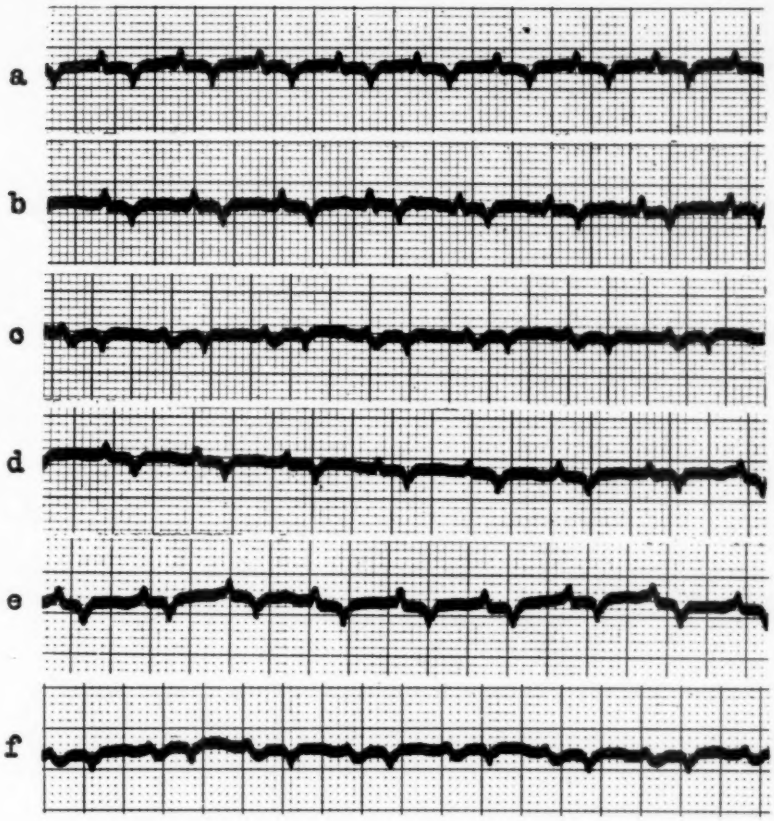

FIG. 2. Case 6; lead V_1. (a) Eighteen minutes after start of NaEDTA infusion. Note slower atrial rate. (b) Twenty-seven minutes after start of NaEDTA infusion. (c) Reappearance of sinus rhythm immediately prior to completion of NaEDTA infusion. (d) Ten minutes after end of infusion. Atrial tachycardia present with 1:1 A-V conduction. (e) Thirty minutes after end of infusion. Atrial rate increased. (f) Sinus rhythm reappearing after institution of potassium chloride therapy.

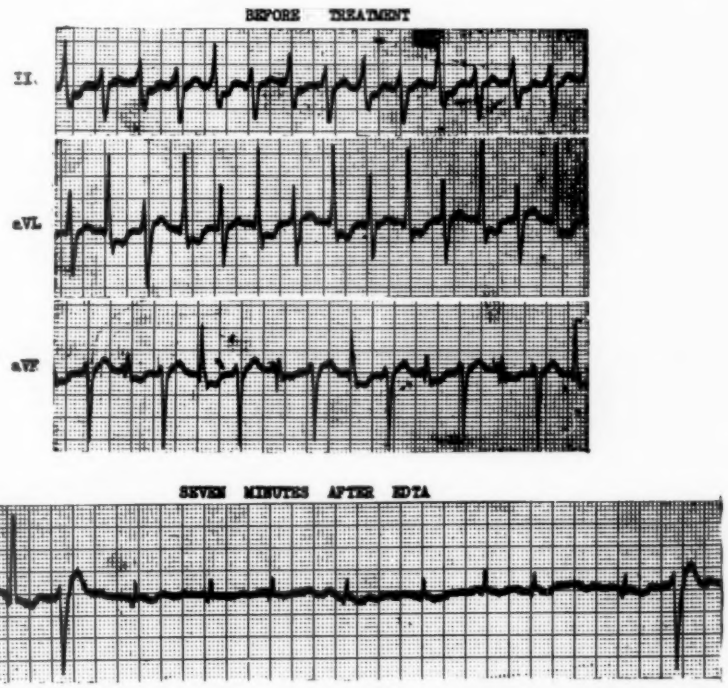

FIG. 3. Case 10 (M. Z.). *Top*, bidirectional tachycardia. *Bottom*, termination of bidirectional rhythm and ree-stablishment of atrial fibrillation seven minutes after beginning of NaEDTA infusion (lead aVL).

in several instances, but in others it did not occur until the entire dose of NaEDTA was given.

NaEDTA therapy was equally effective in arrhythmias and in A-V conduction disturbances associated with digitalis administration. In one of the cases of atrial tachycardia with block, the atrial rate initially slowed and the degree of block lessened prior to the appearance of sinus rhythm—a sequence frequently encountered when potassium is administered in such cases. In some patients (such as in Case 10, reported in detail elsewhere[18]), marked clinical improvement occurred following treatment.

NaEDTA was generally ineffective when given in the absence of digitalis intoxication, although ventricular premature contractions were abolished in one patient on two separate occasions. This patient had received no digitalis and was hospitalized for chronic cholecystitis. She was free of known heart disease. In contrast to the cases of digitalis intoxication, all instances of impaired A-V conduction and one with atrial tachycardia with block were unaffected by the infusion of NaEDTA.

Two cases could not be satisfactorily evaluated for the presence or absence of digitalis intoxication. The possibility exists that digitalis intoxication may have been present in either one or both of these cases and was not altered by calcium chelation. Kabakow and Brothers[7] have presented evidence which suggests that the production of hypocalcemia abolishes digitalis intoxication only in the presence of potassium depletion, and that a favorable response to NaEDTA therapy predicts a subsequent response to supplemental potassium. In neither of these two cases was potassium therapy instituted so the thesis could not be tested.

The dosage of intravenously administered NaEDTA used to abolish digitalis intoxication, and the duration of the infusion, have been variable in published reports. While Gubner and Kallman[13] employed dosages as low as 0.6 gm., single infusions of 4 gm. have been given over a four-hour period.[16] It is desirable that an amount large enough to produce consistent and substantial lowering in the serum calcium be used, and that the administration be rapid enough to properly evaluate any change noted. If several hours are allowed to pass during the infusion, spontaneous electrocardiographic changes will frequently occur unrelated to the treatment. The method we have used fulfills both of the desirable criteria for dosage and duration of administration. Its safety has previously been determined.

While the hypocalcemic effect of NaEDTA therapy is brief, it has not been previously reported that the reversal of digitalis intoxication by the administration of NaEDTA may be of short duration, although this is to be expected. It is evident from our studies that, despite the consistent effectiveness of NaEDTA therapy in cases of digitalis intoxication, the effect may last only several minutes in some instances. The transitory nature of the response, which is probably due to the rapid return of the serum calcium level to normal, somewhat impairs the therapeutic effectiveness of NaEDTA. However, in some cases, the effect was lasting and the clinical status of the patients was greatly improved. NaEDTA would appear to have particular therapeutic value in those cases of digitalis intoxication in which a rapid response is desired.

Although further clinical study is indicated, our results suggest that NaEDTA may also be useful in determining the presence or absence of digitalis intoxication when various arrhythmias and conduction disturbances occur in digitalized patients. The management of cardiac patients who demonstrate electrocardiographic abnormalities consistent with, but not diagnostic of, digitalis intoxication is one of the most difficult therapeutic problems which periodically confronts the physician. Since only one patient in the group without digitalis intoxication showed a marked change following the infusions of NaEDTA, while all the administration of the definitely intoxicated patients showed a pronounced effect, a positive response to the administration of NaEDTA appears to be strongly suggestive of digitalis intoxication, while a negative result casts considerable doubt on its presence. Further study is indicated in order to confirm the validity of this impression.

Summary

1. Sodium versenate (NaEDTA) has been administered intravenously in twenty-seven instances of cardiac arrhythmias or conduction disturbances.

2. In eleven cases the patients were believed to be intoxicated with digitalis. In each case the abnormality was lessened or abolished by the administration of NaEDTA. The beneficial effect lasted only a few minutes in some patients, but was permanent in others.

3. Fourteen instances of similar arrhythmias or conduction disturbances not due to digitalis were also investigated. In one of these cases, ventricular premature contractions were either abolished or diminished in frequency on two separate occasions. In all the other cases in which digitalis intoxication was not present, the electrocardiographic abnormalities were unaffected by the administration of NaEDTA.

4. In two cases in which the presence or absence of digitalis intoxication could not be satisfactorily determined, there was no change following the administration of NaEDTA.

5. NaEDTA, given in the manner described, is a safe and effective therapeutic agent which may be used when rapid reversal of digitalis intoxication is desired.

6. NaEDTA may be useful in determining whether or not a given arrhythmia or conduction disturbance is due to digitalis intoxication.

References

1. Clark, A. J. The influence of ions upon the action of digitalis. *Proc. Royal Soc. Med.*, 5: 181, 1911.
2. Gold, H. and Edwards, D. J. The effects of ouabain on the heart in the presence of hypercalcemia. *Am. Heart J.*, 3: 45, 1927.
3. Baker, J. B. E. Influence of calcium and potassium ions on the toxicity of ouabain. *Brit. J. Pharmacol.*, 2: 259, 1947.
4. Hellems, H. K., Regan, J. J. and Talmus, F. N. Influence of acetyl strophanthidin on myocardial electrolyte exchange. *J. Clin. Invest.*, 34: 915, 1955.
5. Blackman, J. R., Gillespie, L., Berne, R. M. and Hellerstein, H. K. The effects of digitalis glycosides on the electrolyte balance of the myocardium. Alteration of the effects by glucose and insulin and potassium chloride. *J. Lab. & Clin. Med.*, 48: 784, 1956.
6. Loewi, O. On the mechanism of positive isotropic action of fluoride, oleate, and calcium on frog's heart. *J. Pharmacol. & Exper. Therap.*, 114: 90, 1955.
7. Kabakow, B. and Brothers, M. J. The effects of induced hypocalcemia on myocardial irritability and conductivity. *Arch. Int. Med.*, 101: 1029, 1958.
8. Szent-Györgyi, A. Contraction in heart muscle fiber. *Bull. New York Acad. Med.*, 28: 3, 1952.
9. Gubner, R. S. and Kallman, H. Intravenous calcium in acute pulmonary edema. *Circulation*, 14: 946, 1956.
10. Page, E. and Real, D. J. Interrelationships between cardiac effects of ouabain, hypocalcemia and hyperkalemia. *Circulation Res.*, 3: 501, 1955.
11. Nalbandian, R. N., Gordon, S. and Kaufman, J. Calcium-digitalis tolerance test. A clinical report of the first 24 trials. *Am. J. M. Sc.*, 234: 391, 1957.
12. Bower, J. O. and Menger, H. A. K. Additive effect of calcium and digitalis. Warning with report of two deaths. *J. A. M. A.*, 106: 1151, 1936.
13. Gubner, R. S. and Kallman, H. Treatment of digitalis toxicity by chelation of serum calcium. *Am. J. M. Sc.*, 234: 136, 1957.
14. Bessman, S. P. and Doorenhas, N. J. Chelation. *Ann. Int. Med.*, 47: 1036, 1957.
15. Bechtel, J. T., White, J. E. and Estes, E. H., Jr. The electrocardiographic effects of hypocalcemia induced in normal subjects with edathamil disodium. *Circulation*, 13: 837, 1956.
16. Surawicz, B., Kaljot, V., Macdonald, M. G., Lepeschkin, E., Bellinger, J. C. and Bickford, A. Effect of potassium and calcium deficiency on ectopic beats. Abstracts 30th Scientific Sessions Am. Heart Assoc., 1957.
17. Dudley, H. R., Ritchie, A. C., Scheilling, A. and Baker, W. H. Pathologic changes associated with the use of sodium ethylene diamine tetraacetate in the treatment of hypercalcemia. *New England J. Med.*, 252: 331, 1955.
18. Weinstein, W. and Jick, S. Bidirectional tachycardia. *Am. J. Cardiol.*, 3: 343, 1959.

Right Bundle Branch Block with Right Ventricular Hypertrophy*

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IN THE RECENT medical literature,[1–5] there are still very confusing and different opinions of the problems discussed in this paper, namely, the differentiation of right bundle branch block and right ventricular hypertrophy. In this sense, Kossmann,[3] making reference to recent investigations of Bryant, has made the following statement:

"His interesting observations explain in part the chaos which exists with regard to the interpretation of records presumed to indicate block of the right bundle branch, either complete or incomplete, and of records which indicate hypertrophy of the right ventricle."

We believe that three main reasons can explain most of the disagreement and confusion which exist on this subject: (1) Apparently several investigations did not consider the possibility that right bundle branch block and right ventricular hypertrophy could occur at the same time. As we are going to prove in this study, most cases of right ventricular hypertrophy are associated with some degree of right bundle branch block. (2) It would seem that electrogenesis is confused with clinical electrocardiographic interpretation when right bundle branch block and right ventricular hypertrophy are discussed. It has been proved that some electrocardiographic and vectorcardiographic morphologies correspond to right ventricular hypertrophy;[5] this is not a reason, however, to deny some delay in the activation through the right bundle, especially when only distant leads are considered. Direct or intracavitary leads must be obtained to rule out slight degrees of right bundle branch block. (3) There is no clear definition concerning slight degrees of right bundle branch block. It is admitted that the left septal surface becomes activated slightly before the right septal surface. This has been described by Wilson[6] as a slight degree of right bundle branch block occurring in normal hearts.

In man, as well as in the dog, the first part of the ventricle to become depolarized is the midportion of the left septal surface; about 0.01 second later the right septal surface is activated in those portions in which the first ramification of the right bundle branch appear.[7] In view of this experimental knowledge, we would pose a question: When can we speak of slight degrees of right bundle branch block? We admit that the activating impulse is transmitted down the left bundle branch more rapidly than through the right bundle branch. To explain this earlier activation of the left septal surface, we may cite the fact that the left bundle branch ramifies higher in the septum as compared with the right branch.

In this paper we speak of incomplete right bundle branch block when the difference in the beginning of activation of both septal surfaces reaches or exceeds 0.02 second in favor of the left septal surface. Certainly this definition could be modified; but it becomes necessary, as in any other investigation, to have a reference point and this is the one chosen for our investigation.

MATERIAL AND METHODS

This study was carried out on forty patients and, with the exception of two cases, right ventricular hypertrophy was proved in all by clinical radiologic and electrocardiographic methods. In all cases, potential variations from the right atrial and right ventricular cavities were recorded. The distal portion of the catheter (exploring electrode) was manipulated in order to reach the anterior high and low portions of the right septal surface for study of the electrical phenomena corresponding to the right septal mass. It was seen that when the end of the catheter

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was placed near the posterior region of the right septal surface, the potential variation recorded may correspond to the left septal mass instead of the right septal mass. This may lead to an erroneous interpretation concerning the absence of right bundle branch block when actually this represented only an incomplete exploration of the electrical forces of the septum. We have proved that there are portions of the interventricular septum in which the left septal mass, electrically recognized, reaches the right septal surface.[8] These portions are located mainly high and posterior in the septum; in general, in all the muscular portions of the septum behind the moderator band, an important amount of left septal mass is recognized, which may reach the right septal surface at many points. Embryologic and anatomic studies agree with this concept. In favor of this point of view, it was observed that in those cases in which the distal portion of the catheter was moving in the right ventricular cavity, morphologies consistent with those of both the right septal mass and left septal mass were recorded.

In those records obtained at high and low levels near the anterior portion of the right ventricular cavity, the times of onset of the intrinsicoid deflections were measured, and the position of the catheter was controlled by fluoroscopic visualization. The cardiac silhouette was outlined on the surface of the fluoroscopic screen and the varying positons of the catheter were localized by the same method. Attempts were carefully carried out to avoid producing subendocardial injury by pressure of the exploring electrode against the endocardial surface. It should be emphasized that slight or moderate subendocardial injury does not produce any delay in the inscription of the intrinsicoid deflection; in any case, our records show very slight RS-T displacement, so we can rely on the intrinsicoid deflection time.

As discussed previously, we speak of a very slight degree of right bundle branch block when the activation time in the right septal mass reaches or exceeds 0.02 second.

The Sanborn Poly-Viso machine was used to record the morphologies occurring in the right ventricular cavity. The paper speed used was 50 mm./second. There has been some discussion criticizing the use of the direct writing machines; however, after several years of experience with cathode ray oscillographs, we find there is very little difference in the measurement of the intrinsicoid deflection time with both machines. All the intracavitary recordings were obtained simultaneously with lead V_1, and in eleven patients vectorcardiographic studies in the horizontal plane were performed.

Results

The tracings were divided into three groups according to the timing of the intrinsicoid deflection.

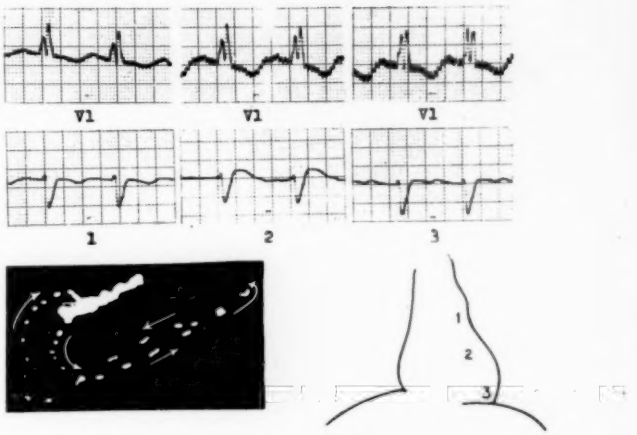

Fig. 1. Right ventricular intracavitary leads recorded simultaneously with V_1 at points 1, 2 and 3 shown on cardiac silhouette. In this case no right bundle branch block was demonstrated by the intracavitary leads, although in V_1 there are two positivities. The horizontal vector loop is suggestive of right bundle branch block.

Group I (Six Cases): The time of the intrinsicoid deflection of these tracings was less than 0.02 second. In these cases, there probably was no right bundle branch block, and we say probably because of the possibility of recording the morphology of the left septal mass instead of that of the right.

In this group, the QRS morphologies in lead V_1 were RsR (one case), qRs (one case), qR (two cases), and rsR′ (two cases). Figure 1 shows one of the cases with an M morphology in lead V_1 in which we could not demonstrate a delay in the activation of the right septal mass in the intracavitary studies; the three intracavitary tracings are of the rS type with an inscription of the intrinsicoid deflection below 0.02 second. It is possible that in these cases the right septal mass was not explored; in favor of this point of view is the horizontal vectorcardiographic loop presented in the same figure which is very similar to that of other cases in which right bundle branch block was proved.

Group II (Seventeen Cases): In this group the time of inscription of the intrinsicoid deflection of the intracavitary tracings varied between 0.02 and 0.039 second. These cases correspond to slight degrees of right bundle branch block. The QRS morphologies in lead V_1 were: Rs (four cases); rsR (three cases); R with initial slurring on the upstroke (four cases); R with slurring at the apex (three cases); qR (two cases); and R (one case).

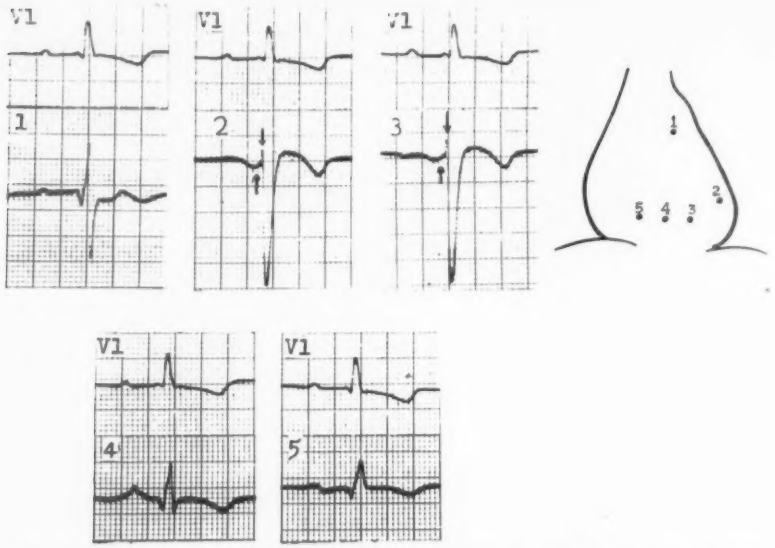

FIG. 2. Slight degree of right bundle branch block. Note the small initial positivity in V_1 which is synchronous with a similar initial positivity in the intraventricular tracings obtained at points 2 and 3.

Figure 2 shows intracavitary tracings of a thirty-three year old patient with chronic cor pulmonale. The morphologies obtained at points 2 and 3, near the regions in which the first ramifications of the right bundle branch begin, are of the rS type with an initial slurring. Due to this slurring the superior vertex of the intrinsicoid deflection is inscribed at 0.025 second, corresponding to a slight degree of right bundle branch block according to our criteria. This initial slurring is inscribed simultaneously with a small positivity in lead V_1 which precedes the more important positive deflection in this lead; note that the duration of the QRS is only 0.08 to 0.09 second. At point 4 of Figure 2 the superior vertex of the intrinsicoid deflection is inscribed at 0.04 second and the same inscription time is obtained at point 1 located immediately below the pulmonary valve. This tracing suggests that other high portions of the right

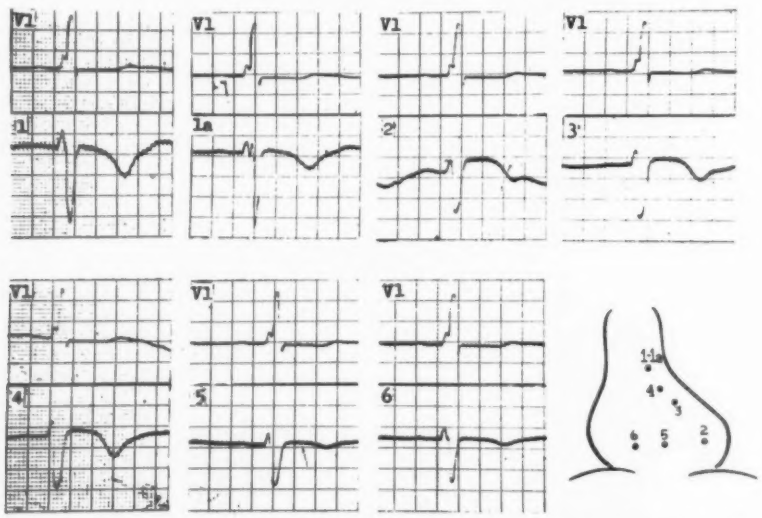

FIG. 3. Slight degree of right bundle branch block. In V_1 the tracing is of the Rs type with a small positive initial slurring, which is synchronous with a similar initial slurring in most of the intracavitary tracings. Some of the complexes shown for V_1 are retouched.

septal mass are activated after the regions explored at points 2 and 3.

The intracavitary tracings shown in Figure 3 are those of a sixteen year old girl with tetralogy of Fallot. In lead V_1 the tracing is of the Rs type, with a small positive initial slurring indicating a tendency to the inscription of two positivities. The intracavitary leads at points 2 to 6 all show the same type of complexes, that is, an rS in which the initial positivity is synchronous with the initial slurring of the R in lead V_1. The intrinsicoid deflection of all these records is inscribed at about 0.025 second; however, at point 6 the intrinsicoid deflection was written later.

Exploring the high portions of the right septal mass in this case, the intrinsicoid deflection is inscribed still later (at 0.052 second at point 1, Figure 3). We may speak then of a mild degree of right bundle branch block. The delayed septal activation produces the slurred initial positivity of the intracavitary tracings and the initial slurring of R in lead V_1. The remainder of the QRS deflection lead in V_1, that is, the R wave after the slurring, corresponds probably to the activation forces across the free right ventricular wall, since it is synchronous with the S wave of the intracavitary tracings.

This is a definite instance in which it is possible to recognize a slight degree of right bundle branch block by the slurring in lead V_1; also, the right ventricular hypertrophy could be diagnosed by the high R wave inscribed after the slurring in the same right precordial lead V_1.

Group III (Seventeen Cases): In this group the time of onset of intrinsicoid deflection of the intracavitary tracing varies between 0.040 and 0.11 second. These cases correspond to moderate to severe degrees of right bundle branch block. In lead V_1, the following morphologies were recorded: R with notchings and slurrings at the vertex (three cases); rsR′ (eight cases); qR (one case); RsR′ (one case); and Rs (four cases).

Figure 4 shows a tracing of a thirty-three year old man on whom a commissurotomy and left pneumonectomy were performed for mitral stenosis and tuberculosis, respectively. The tracing corresponds to a medium degree of right bundle branch block; we speak of a medium degree owing to a definite delay in the inscription of the intracavitary tracing, but this delay is not as striking as in cases of complete right bundle branch block. In the low levels of the right ventricular cavity (point 3, Figure 4), the

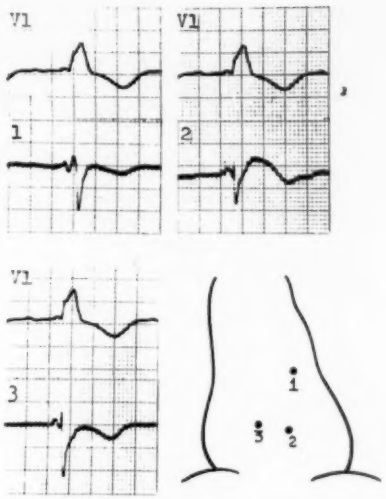

FIG. 4. Medium degree of right bundle branch block. Note that the intrinsicoid deflection of the intracavitary tracings is inscribed at 0.04 second at the low levels of the cavity (points 2 and 3) while the same deflection is inscribed at 0.06 second in the tracings obtained at higher levels (point 1).

intrinsicoid deflection is inscribed at 0.04 second while in the high portions of the cavity (point 1) it is inscribed later at 0.06 second. Note that in the intracavitary tracings as well as in lead V_1, there is an initial slurred small positivity which suggests a slow activation across the septum (physiologic barrier). In the intracavitary tracings, a rapid second positivity synchronous with the first portion of the upstroke of the R wave in lead V_1 is inscribed; this synchronism suggests the septal origin of the second positivity. In the high intracavitary leads of the same case (point 1, Figure 4) the second R deflection is also slurred. As we have described in previous reports, this is suggestive of a slow activation through the right septal mass. The only part of the deflection that could be ascribed to the activation of the free right ventricular wall is the final portion of the R′ in lead V_1.

In Figure 5, the intracavitary tracings of an eighteen year old girl with double mitral and aortic valve lesions are shown. The hemodynamic study indicated that the area of the mitral valve was 0.46 sq. cm., the right ventricular systolic pressure 83.4 mm. Hg, total pulmonary resistance 1,740 dynes/second/cm.$^{-5}$ and pulmonary arterial resistance 1,040 dynes/second cm.$^{-5}$. In this case, there is a greater degree of right bundle branch block: the low intracavitary tracings (points 3 and 4, Figure 5) show an RS complex with inscription of the

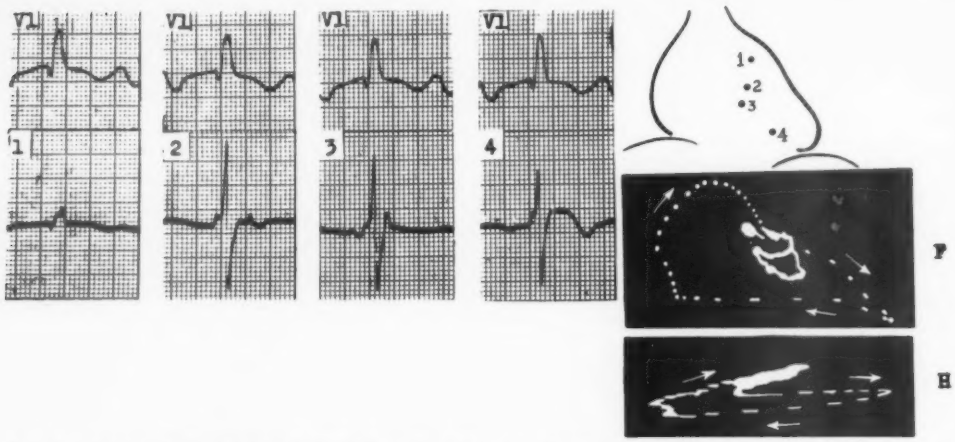

FIG. 5. Severe degree of right bundle branch block. The intrinsicoid deflection is delayed (0.05 second) in all the intracavitary tracings and in V_1. The frontal and horizontal vector loops also show conduction delay.

upper vertex of the intrinsicoid deflection at 0.05 second. In the high intracavitary location (point 1, Figure 5) the tracing becomes rsR′ and the intrinsicoid deflection is inscribed even later than in the precordial lead V_1. In this lead, the tracing is of the qR type sometimes, and at other times, rSR′ type, and the R′ is synchronous with the R′ at point 1 of the intracavitary tracing; in other words, the two late R waves (intracavitary and extracavitary) are produced by the same electrical force. This force has been referred to as the electrical activity of the free right ventricular wall by Bryant,[2] who invokes an activation front perpendicular to the endocardial and epicardial surface and going from apex to base. We ascribe this force to the activation of the right septal mass from below upward since the total extirpation of the free right ventricular wall does not prevent this morphology from being recorded.[11]

The tracings of Figure 6 were obtained in a nine year old boy with rheumatic myocarditis and mitral insufficiency. The morphology in lead V_1 is characteristic of a marked degree of right bundle branch block. The intracavitary tracings near the low right septal mass (point 2, Figure 6) show a significant delay in septal activation (0.06 second) and the tracing is of the rsr′R″S″ type. The R″ is synchronous with the first portion of the upstroke of the R′ in lead V_1 which suggests, as in the previous experiments, the septal origin of the two positivities.

COMMENTS

We have defined as the slightest degree of right bundle branch block those cases in which

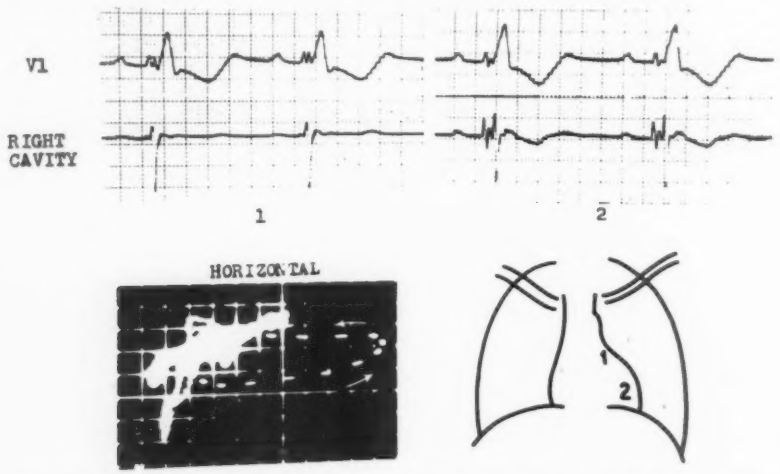

FIG. 6. Advanced degree of right bundle branch block. In the low intracavitary tracings (point 2) the intrinsicoid deflection is inscribed at 0.06 second.

the right septal surface is activated 0.02 second or more after the beginning of the activation of the left septal surface. With this criterion, we have shown in this study that of thirty-eight patients with right ventricular hypertrophy thirty-four had evidence of some degree of right bundle branch block. There is no reason to put one diagnosis against another as many authors do; the presence of one does not exclude the other. Neither is there reason to speak of chaos in this type of investigation. The solution of the problem is obtained by taking a reference point as we have done in this investigation. We will discuss some points closely related with this study on which there is still considerable discussion in the literature.

The Activation of the Right Septal Mass in Right Bundle Branch Block: In all intracavitary tracings taken during this investigation, it was noted that the high septal mass was activated later than the low septal mass. Similar results had been previously obtained in the dog's heart in our laboratory. Scher and his group[9] state that the activation across the septum is uniform. We cannot accept this viewpoint inasmuch as notching and slurring of the tracings obtained from the high and low right septal masses are proof against their conclusion. These notchings and slurrings are due to a slow transseptal activation and cannot be ascribed to activation of the free right ventricular wall since they still remain after total extirpation of this wall.[11]

The Recognition of Right Ventricular Hypertrophy in the Presence of Right Bundle Branch Block: We may say, in general, that when there is right axis deviation between +120 and +180 degrees in the presence of right bundle branch block, the possibility of right ventricular hypertrophy becomes strong; nevertheless, we do not believe this is the most accurate means of arriving at this conclusion. The analysis of the morphologies in the unipolar precordial leads will give a more precise answer.

In Figure 7 are shown the most important unipolar ventricular morphologies seen in right bundle branch block. These correspond to the right atrium (A), free right ventricular wall (B), trabecular zone of the right ventricle (C), low septal portions belonging to the right septal mass (D), and the free wall of the left ventricle (E).

We have noted that some investigators[2] have not given sufficient importance to the study of these morphologies and interpret some tracings as though they correspond to block of the two

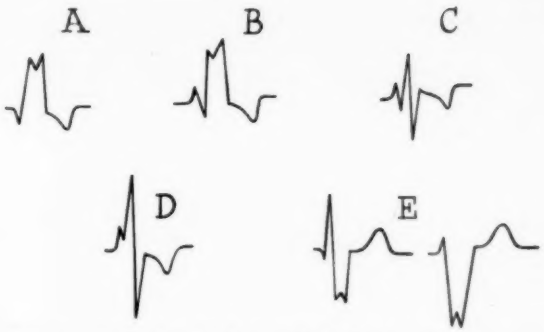

FIG. 7. Unipolar lead morphologies commonly seen in right bundle branch block. They reflect the potential variations of: A, right atrium; B, free right ventricular wall; C, trabecular zone of the right ventricle; D, low right septal mass; and E, free left ventricular wall.

branches of the bundle of His, inasmuch as the intrinsicoid deflection was delayed on both sides of the precordium; what really happens is that the right ventricle occupies the whole anterior aspect of the heart. In Figure 8 the morphology registered in lead V_1 is of the qR type with a negative T wave; in leads V_2 and V_3 the complexes are of the qRs type, also with a negative T wave. We have described these morphologies as corresponding to the potential variations (not to be mistaken with action potential) of the

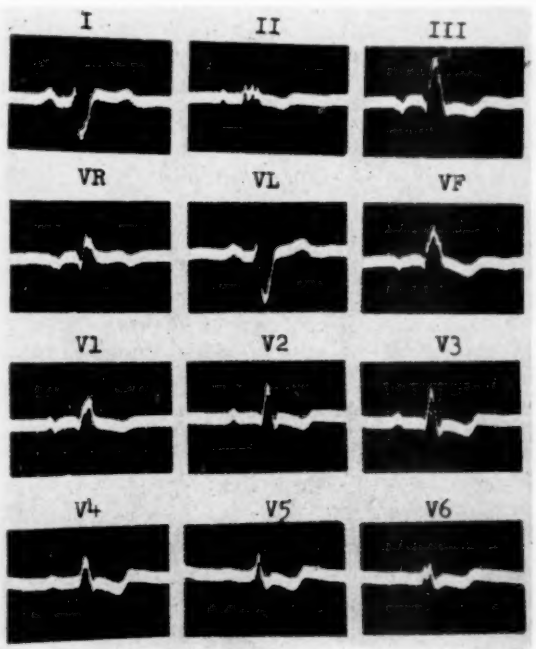

FIG. 8. In this tracing the unipolar lead morphologies of the right atrium are inscribed from V_1 through V_3; those of the free right ventricular wall in V_4 and V_5 and that of the low septal mass in V_6.

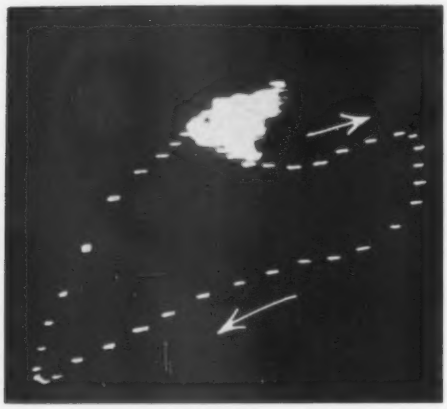

FIG. 9. The vectorcardiographic loop in the horizontal plane shows clockwise rotation which has been interpreted by some investigators as corresponding to right ventricular hypertrophy. The orientation of the loop depends more on the block than on the hypertrophy, and for this reason it changes when the block diminishes, as is seen in Figure 11. This loop has been retouched.

FIG. 10. This form of vector loop in the horizonta plane is the most common in right bundle branch block without ventricular hypertrophy. It shows clockwise rotation, figure-of-eight configuration and conduction delay.

right atrium or of very high portions of the free right ventricular wall near the anterior A-V groove. The complexes from leads V_4 through V_6 are of the Rs type with a negative T wave, corresponding to potential variations of the free right ventricular wall and, in the case of lead V_6, very probably to the right lower septal mass. In other words, we are exploring through the precordial leads regions proximal to the right atrium and right ventricle. The left ventricle is explored only in aVL and in lead I, in which the morphology of the ventricular complex is of the rS type, with early inscription of the intrinsicoid deflection and a positive T wave (Fig. 8).

Right Bundle Branch Block and the Horizontal Vectorcardiogram: Some authors have claimed that vectorcardiogram morphologies similar to those seen in Figures 9 and 10 correspond to right ventricular hypertrophy. In accordance with this point of view the diagnosis of right bundle branch block would be ruled out. In these cases, however, the right intracavitary study near the right septal mass proves that in addition to the right ventricular hypertrophy there is also slight or advanced degree of right bundle branch block.

Three main types of vectorcardiographic loops can be recognized in cases of right bundle branch block:

(1) The first type (Fig. 10) corresponds to right bundle branch block without ventricular hypertrophy and is commonly seen in patients with coronary atherosclerosis.

(2) In the second type (Fig. 9), there is right ventricular hypertrophy in addition to the block but the morphology of the loop depends more on the block than on the hypertrophy; this statement is based on the fact that when the block disappears the vectorcardiographic morphology changes. This has been noted in some curves that were kindly sent to us by Gardberg[12] (Fig. 11).

(3) In the third type (Fig. 12), the heart is

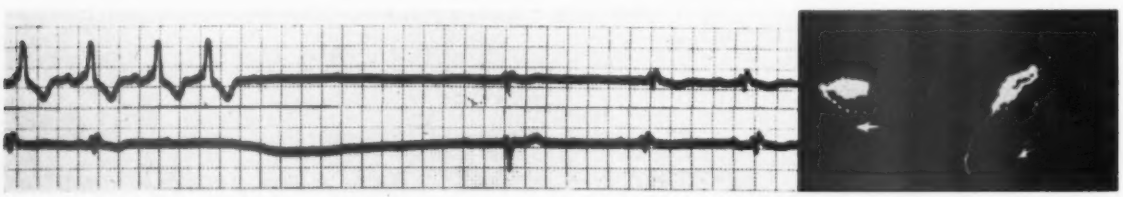

FIG. 11. This tracing was kindly sent to us by Gardberg.[12] Note the important change of the vectorcardiographic loop in the horizontal plane when the degree of right bundle branch block in V_1 diminishes following carotid sinus pressure.

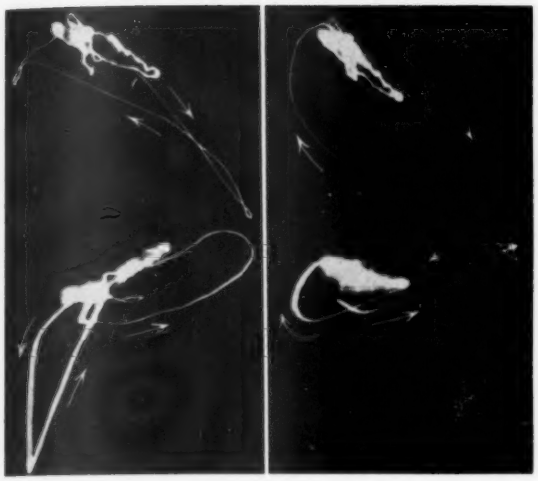

FIG. 12. Vectorcardiogram in varying degrees of right bundle branch block. The upper loops in both columns correspond to the frontal plane while the lower loops correspond to the horizontal plane. Note the important changes in the right column when the degree of right bundle branch block diminishes.

generally normal although there are some cases in which left ventricular hypertrophy is present. In Figure 12, the vectorcardiographic loop changes importantly when the degree of right bundle branch block diminishes. These changes are important evidence in favor of the block.

SUMMARY

Thirty-eight cases of proved right ventricular hypertrophy were studied. Right intracavitary leads obtained near the anterior papillary muscle demonstrated some degree of right bundle branch block in addition to the hypertrophy in thirty-four of the cases. The block was mild in seventeen cases (intrinsicoid deflection between 0.02 and 0.039 second) and severe in seventeen cases (intrinsicoid deflection between 0.04 and 0.11 second). It is also emphasized that analysis of the morphologies in the intracavitary and precordial leads may aid in the recognition of right ventricular hypertrophy in the presence of right bundle branch block.

REFERENCES

1. KOSSMANN, C. E. Advances in Electrocardiography. New York, 1958. Grune & Stratton.
2. BRYANT, M. J. Intraventricular conduction. In: Advances in Electrocardiography. Edited by Kossmann, C. E. New York, 1958. Grune & Stratton.
3. KOSSMANN, C. E. The effect of myocardial disease and dysfunction on the form of the electrocardiogram. In: Transactions of the Association of Life Insurance Medical Directors of America (Sixty-Sixth Annual Meeting), vol. 41. Edited by Gudger, J. R. New York, 1958. Recording and Statistical Corporation Press.
4. DICKENS, J. and GOLDBERG, H. Correlation of the precordial and endocardial ventricular electrocardiogram. *Am. Heart J.*, 56: 8, 1958.
5. GRISHMAN, A. and SCHERLIS, L. Spatial Vectorcardiography. Philadelphia, 1952. W. B. Saunders Co.
6. WILSON, F. N., JOHNSTON, F. D., ROSENBAUM, F. F., EARLANGER, H., KOSSMANN, C. E., HECHT, H., COTRIM, N., MENEZES DE OLIVEIRA, R., SCARSI, R. and BARKER, P. S. The precordial electrocardiogram. In: Selected Papers of Dr. Frank N. Wilson. Ann Arbor, Mich., 1954. Heart Station, University of Michigan Hospital.
7. SODI-PALLARES, D. New Bases of Electrocardiography. St. Louis, 1956. C. V. Mosby Co.
8. MEDRANO, G. A., PILEGGI, F., SOTOMAYOR, A., BISTENI, A. and SODI-PALLARES, D. Neuvas investigaciones sobre la activacion de septum interventricular en condiciones normales y con bloqueo de rama. Parte I. Estudio de al porcion posterobasal del tabique. *Arch. Inst. cardiol. Mexico*, 26: 616, 1956.
9. SCHER, A. M., YOUNG, A. C., MALGREN, A. D. and ERIKSON, R. V. The activation of the interventricular septum. *Circulation*, 3: 56, 1955.
10. MIQUEL, C., SODI-PALLARES, D., CISNEROS, F., PILEGGI, F., MEDRANO, G. A. and BISTENI, A. Right bundle branch block and right ventricular hypertrophy. *Am. J. Cardiol.*, 1: 57, 1958.
11. MEDRANO, G. A., SODI-PALLARES, D., MARSICO, F. and BISTENI, A. The importance of septal activation in the electrogenesis of the unipolar morphologies in bundle branch block. *Am. Heart J.*, 57: 126, 1959.
12. GARDBERG, M. and ROSEN, I. L. The cube vectorcardiogram in various degrees of right bundle branch block. *Am. J. Cardiol.*, 2: 572, 1958.

Intermittent Right Bundle Branch Block Without Apparent Heart Disease*

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THE OPINION persists that intermittent bundle branch block is a manifestation of underlying heart disease. Recently, Shearn and Rytand[1] concluded a study of eight cases of intermittent bundle branch block by stating "It appears that intermittent bundle branch block is usually an expression of underlying myocardial disease and probably represents a transitional stage before permanent bundle branch block supervenes." This point of view is hardly surprising since the average cardiac patient presenting himself to the clinician has some medical reason for seeking consultation in the first place. In the series of Shearn and Rytand, all subjects were of an older age group and all eight cases reported were of complete left bundle branch block. Similar clinical studies in older age groups are encountered in the literature and in each instance, the authors have come to a similar conclusion. Comeau, Hamilton and White[2] reported thirteen cases of intermittent block and reviewed the reported cases (fifty-eight) available at that time. They concluded that intermittent bundle branch block was usually a sign of serious heart disease.

Intermittent bundle branch block was first described by Lewis in 1910.[3] Wilson and Herrmann[4] first reported the relationship of respiration to the intermittent character of left bundle branch block in 1923. Cardiac rate, as a factor in the intermittent character of bundle branch block, was noted by Baker[5] in 1930. He observed that oxygen inhalation resulted in decreased cardiac rate and normal sinus rhythm. He thought that oxygen diminished the demand for increased cardiac output and enabled the bundle to conduct impulses in a more normal fashion.

Vesell[6] emphasized the critical heart rate as related to intermittent bundle branch block. Although recognizing the cardiac rate as a critical factor, he still attributed the intermittent block to underlying cardiac disease. Later[7] he reported a ten year follow-up on a case of intermittent bundle branch block and old myocardial infarction.

One case of a fifty-six year old woman with hypertension and intermittent right bundle branch block was reported by Lasser and Grishman.[8] They also noted that bundle branch block appeared when the cardiac rate was increased. No intermediate forms in transition were noted. More recently Gardberg and Rosen[9] reported a case of intermittent right bundle branch block with intermediate degrees of block in a seventy-four year old man.

There are several reported instances of reversal to normal conduction some time after bundle branch block was noted. Digilio[10] reported reversal of left bundle branch block to normal conduction following correction of thyrotoxicosis. A review of the published records demonstrated a marked difference in cardiac rate before and after treatment. Kalett[11] reported spontaneous remission of left. bundle branch block four years after it was first noted in a fifty-six year old Major.

Boyadjian and van Dooren[12] published interesting examples of conversion of bundle branch block following the long pause immediately after a premature contraction.

There are only occasional case reports in the literature exemplifying intermittent or transient

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bundle branch block in apparently healthy subjects. One such case was reported by Sandberg et al.[13] of a twenty-two year old nurse with intermittent complete right bundle branch block. No relationship to change in the cardiac rate could be detected. Nichols[14] reported an excellent example of intermittent right bundle branch block as related to cardiac rate and vagal influences in an apparently healthy twenty-eight year old infantryman.

Recent experiences in our laboratory in the evaluation of relatively asymptomatic persons on full military duty, who present with the finding of intermittent bundle branch block, have led us to challenge some of the classic clinical concepts which are held in regard to intermittent bundle branch block. This report will deal with four subjects with intermittent right bundle branch block with no evidence of heart disease, and two subjects with intermittent left bundle branch block with heart disease. In all instances, the presence of right bundle branch block was distinctly related to cardiac rate. By use of vectorcardiographic technics and oscillographic recordings in the presence of intermittent block, we have been forced to the conclusion that the change in order of excitation in intermittent complete right bundle branch block is not similar to the change in order of excitation encountered in intermittent complete left bundle branch block. The frequency of intermittent left bundle branch block in the reported literature in association with underlying heart disease as compared with the relative infrequency of intermittent right bundle branch block has led us to believe that the report of these cases may help to lift the veil of suspicion that shrouds the apparently healthy person who presents with intermittent complete right bundle branch block.

Case Reports

Case 1. This thirty-six year old officer was evaluated at the School of Aviation Medicine on March 6, 1957. A normal electrocardiogram was recorded on January 25, 1955. The reason for the recording of the electrocardiogram is unknown. As a child, he had had several electrocardiograms because he had a "high pulse rate." Reportedly, all electrocardiograms were normal. He gave no past history or symptoms referable to rheumatic fever or other forms of heart disease.

In June 1956, the patient's leg muscles ached following moving furniture. In July, he had swelling of the middle fingers of both hands. He sought medical attention for this difficulty in September but x-ray examination of his hands showed no significant findings. He also had aching pain in the right knee and later migratory pain developed of the neck and jaw which was not associated with exercise.

An electrocardiogram recorded on September 28, 1956 showed complete right bundle branch block. Laboratory studies of that date were as follows: white blood cells, 5,200 per cu. mm. with a normal differential; red blood cells, 4,950,000 per cu. mm.; sedimentation rate, 10 mm./hour; C-reactive protein, negative; and antistreptolysin titer, less than 12 units. Agglutination studies and urinalysis were within normal limits as was the chest roentgenogram.

At the time of consultation, the patient was asymptomatic. He gave no history relative to coronary insufficiency, and had a normal exercise tolerance test. He blamed his difficulty on innoculations received in the fall of 1955 and repeated in March and September 1956. He gave a past history of sensitivity to immunizations manifested by an urticarial reaction of fourteen days' duration in 1944. Following the innoculations in 1955 and 1956, there was no rash, fever or other evidences of sensitivity reaction. There were no other significant findings on system review. The family history was not significant.

On physical examination, he was noted to be 5 feet, 8 inches tall and weighed 180 pounds. The cardiac sounds were entirely normal. The blood pressure was 130/80 mm. Hg. Complete laboratory studies including hemogram, sedimentation rate, fasting blood sugar, uric acid, bromsulphalein test and urinalysis were entirely within normal limits. The chest roentgenogram revealed no abnormalities.

Pulmonary function studies were performed which

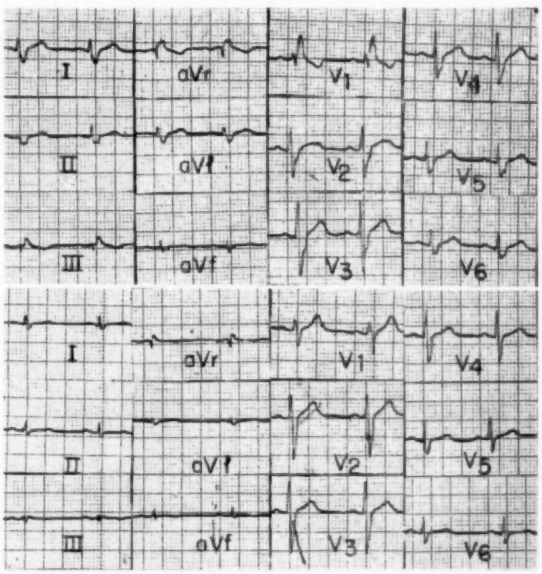

Fig. 1. Case 1. Complete right bundle branch block (*upper*) and normal conduction (*lower*) in the same subject.

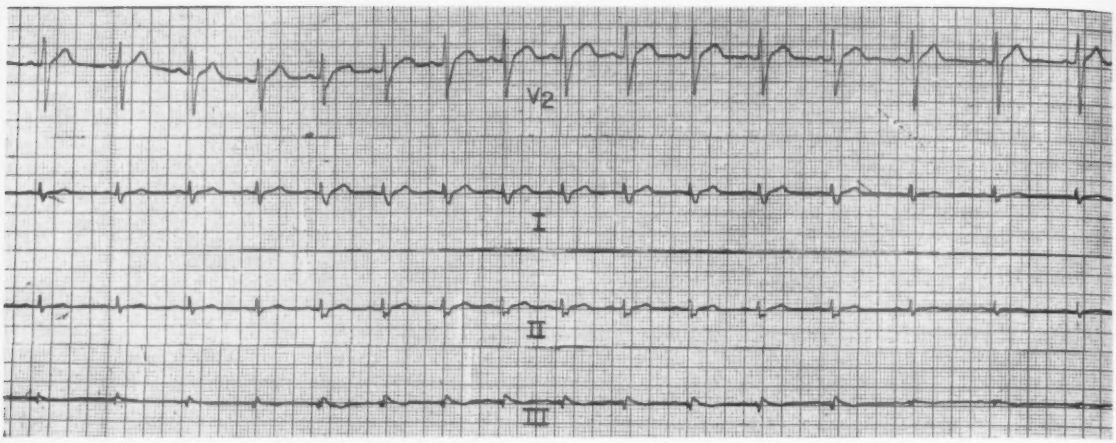

FIG. 2. Case 1. Simultaneous recording of leads V_2, I, II and III demonstrating onset of complete bundle branch block during the inspiratory phase of respiration with increased heart rate and conversion to normal conduction with the expiratory phase. Note the changes with intermittent block are in the terminal portion of QRS cycle.

showed that the vital capacity was 4,750 cc. and the timed vital capacity normal.

An electrocardiogram revealed the presence of complete right bundle branch block as manifested by a broad S wave in lead I and rR′ complex at V_1. During the recording of the routine tracing, it was noted that a marked change in the electrocardiogram occurred during expiration. This change was due to apparent normal intraventricular conduction (Figs. 1 and 2). During the time of nearly normal intraventricular conduction, the RR interval was only slightly longer than that noted in the presence of complete right bundle branch block. Thus, slight slowing of cardiac rate was associated with conversion to normal intraventricular conduction.

Comment: It was interesting to note that the principal change in the electrocardiogram in the presence of right bundle branch block appeared to be in the terminal portion of the QRS complex. The initial part of the QRS complex remained the same with either normal conduction or in the presence of complete right bundle branch block. The restriction of the change in the QRS complex to the terminal portion of ventricular excitation suggested to us at the time that this type of right bundle branch block may indeed be associated only with terminal events of ventricular excitation without any significant change in the early order of excitation. This in turn suggests that even in the presence of right bundle branch block, the septum and main portions of the endocardial shells of both ventricles must undergo their usual normal sequence of excitation.

In the presence of an isolated finding of intermittent complete right bundle branch block in a thirty-six year old, asymptomatic subject, it was not thought justifiable to classify this person as having significant underlying heart disease. His exercise tolerance and daily pattern of living hardly suggested the necessity of restrictions imposed on cardiac invalids. Accordingly, he was advised to continue normal living.

CASE 2. This twenty-four year old pilot was a person who prided himself on his physical condition and frequently engaged in weight lifting activities and other athletic sports. He was evaluated at the School of Aviation Medicine due to two syncopal episodes and the finding was intermittent right bundle branch block. He stated that in the early part of 1956 he was somewhat below his usual topnotch physical condition. This was brought about by lack of exercise, excessive smoking and occasional alcoholic drinks to which he was unaccustomed. On April 17, 1956, he had a slight sore throat of enough magnitude to consult his flight surgeon. In May 1956, he had an unexplained episode of fever and chills. For this, he went to bed for only a matter of hours. There were no associated joint pains, sore throat, rash or skin nodules. On June 18, 1956, he had his annual physical examination which he passed without difficulty.

In mid-June 1956, he experienced his first episode of syncope. This occurred following a light breakfast and his morning shower. He had returned to his bedroom and felt slightly dizzy and apparently fell to the floor. His total duration of unconsciousness was probably less than ten seconds. On regaining consciousness, he felt tired and somewhat nauseated. Approximately two weeks later, after recurrent fatiguing flying missions, he returned home and while waiting for his wife to prepare his evening meal, suddenly became dizzy and had a syncopal episode. He recovered rapidly and has remained relatively asymptomatic since that time. Three days following his second syn-

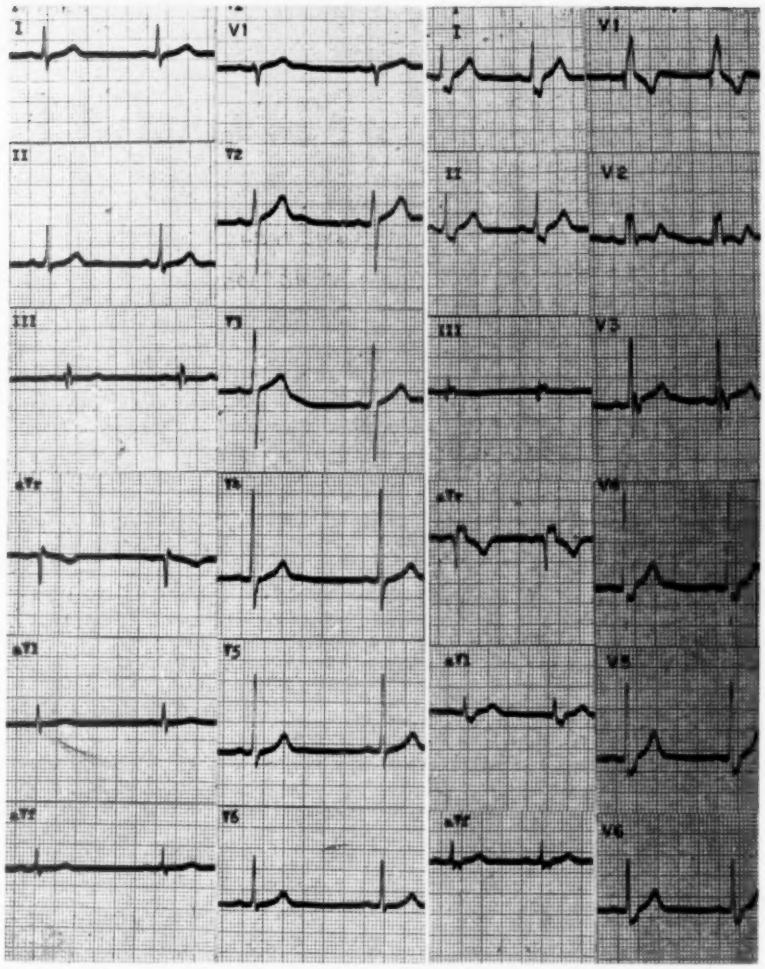

FIG. 3. Case 2. Normal conduction (*left*) with a cardiac rate below the critical level and complete right bundle branch block (*right*) with a slight increase in heart rate (from 48 to 65 per minute).

copal episode, he was seen by his flight surgeon. The physical examination was non-contributory. An electrocardiogram was recorded for the first time on this examination. It demonstrated complete right bundle branch block. The patient had no previous electrocardiograms for comparison. The record was repeated a few days later and the right bundle branch block still persisted. There were no other findings on either physical or laboratory examination. In October 1956, an electroencephalogram was performed which was normal.

A year later, the patient took a physical examination for air traffic control school. Since his previous difficulty, he had improved his physical condition by increased athletic activity. He had given up smoking and desisted from what little alcohol he had previously imbibed. As part of his physical examination an electrocardiogram was performed which was entirely normal. A subsequent electrocardiogram was likewise normal. He was then referred to the School of Aviation Medicine for evaluation of his intermittent right bundle branch block and his two earlier syncopal episodes.

On interrogation, he was asymptomatic and presented as a robust healthy, young man without complaint. He had no pertinent history other than that outlined. The family history was non-contributory.

On examination, the patient was 5 feet, 11 inches tall and weighed 180 pounds; blood pressure was 120/70 mm. Hg.; pulse, 72 and regular. On auscultation a soft apical systolic murmur could be heard near the fourth left intercostal space with the patient in the left lateral position (functional murmur). No other significant findings were noted.

Laboratory studies were as follows: hemogram, normal; sedimentation rate, 2 mm.; urinalysis, normal; fasting blood sugar, 91.4 mg. per cent; antistreptolysin titer, 12 units; blood cholesterol, 202 mg. per cent; phospholipids, 250 mg. per cent; S_f 0–12, 283 mg. per cent, S_f 12–20, 37 mg. per cent; S_f 20–

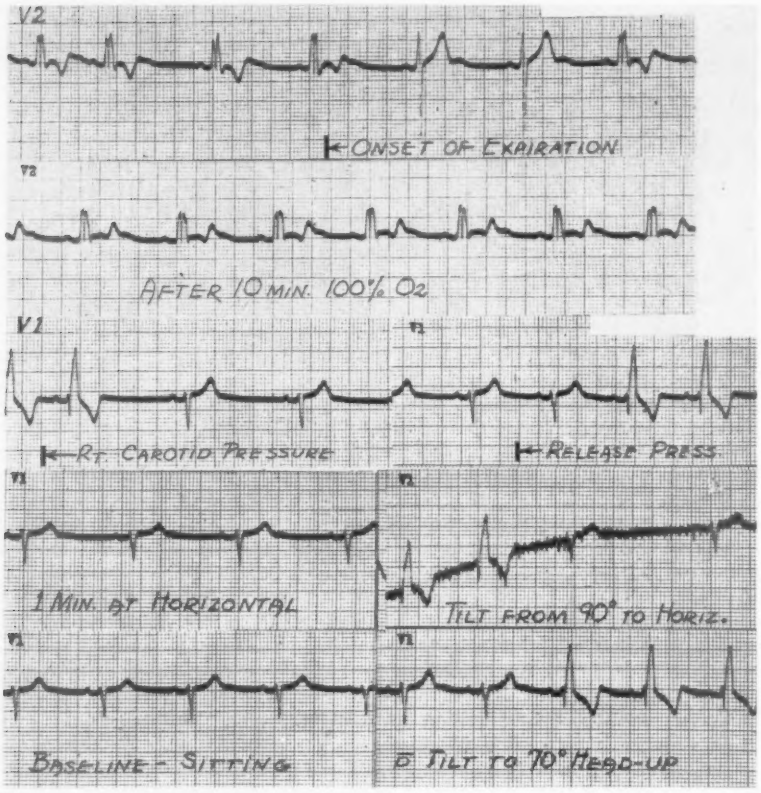

FIG. 4. Case 2. This figures illustrate a few of the methods used to control the character of intermittent bundle branch block in this case, such as deep breathing, breath holding, 100 per cent oxygen inhalation, carotid sinus pressure and changes in body position. In all these maneuvers the heart rate is the critical factor.

400, 41 mg. per cent; Gofman atherogenic index, 42.

Pulmonary function studies were performed and the vital capacity was 4,681 cc. (104 per cent of normal); maximal breathing capacity, 185 L. per minute; the timed vital capacity was as follows: one second, 74 per cent; two seconds, 94 per cent; three seconds, 99 per cent.

The initial electrocardiographic record demonstrated a sinus rate of approximately 65 per minute with complete right bundle branch block (Fig. 3). This unexpected finding led to the review of all his previous tracings which demonstrated that in both instances, when normal electrocardiograms had previously been recorded, the cardiac rate was below 60 per minute. This suggested that the intermittent right bundle branch block was a function of critical heart rate. Subsequent evaluation demonstrated that the cardiac rate could be controlled by simple respiratory maneuvers and by such a mechanism with cardiac slowing, a normal electrocardiogram could be recorded.

Having identified the normal conduction and intermittent complete right bundle branch block as a function of cardiac rate, this hypothesis was then subjected to evaluation by a number of different procedures (Fig. 4). It was demonstrated that during the expiratory phase of normal deep breathing, normal intraventricular conduction could be produced. Another means of producing normal conduction was to hold the breath at the height of inspiration. Carotid sinus massage with cardiac slowing resulted in normal intraventricular conduction. Following release of carotid stimulation, cardiac rate increased with subsequent return to complete right bundle branch block. Simple tilting procedures associated with changing cardiac rate resulted in changes in intraventricular conduction. In the horizontal position, with a relatively slow cardiac rate, normal intraventricular conduction was present. By tilting to a 70 or 90 degree position, increased cardiac rate was associated with right bundle branch block. The patient breathed 100 per cent oxygen for a period of ten minutes and demonstrated the persistence of complete right bundle branch block when the cardiac rate was approximately 60 per minute.

A quantitative vectorcardiogram was recorded in the presence of complete right bundle branch block and in the presence of normal intraventricular conduction. The use of the cathode ray oscilloscope and recording of the three mutually perpendicular planes in the presence of normal and abnormal conduction

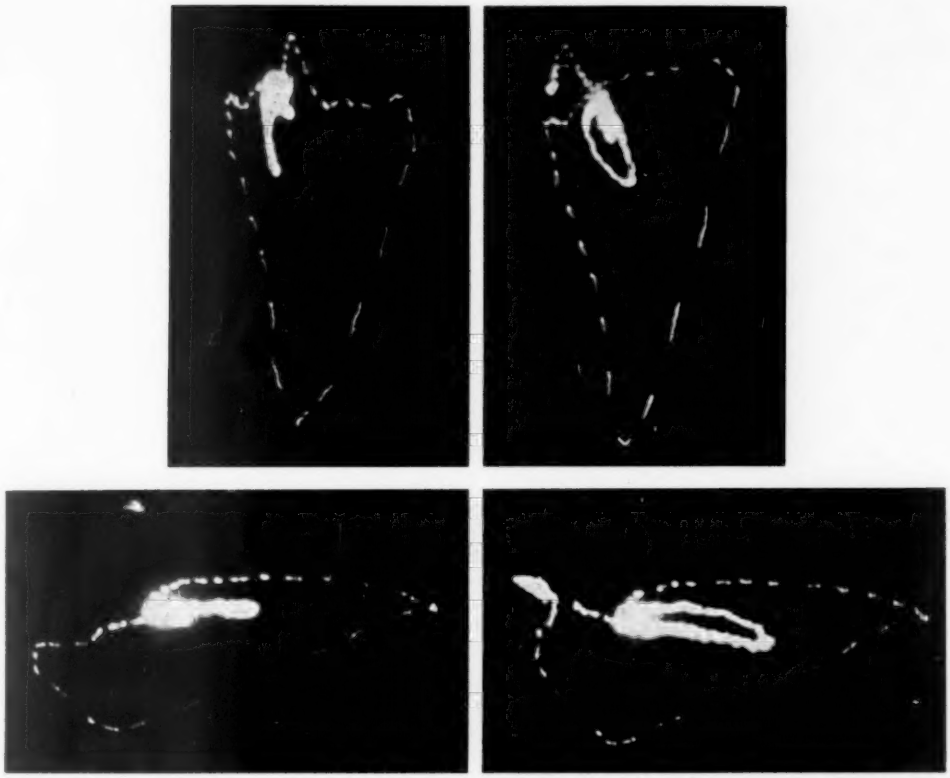

FIG. 5. Case 2. Vectorcardiographic loops. *Upper left*, sagittal plane in normal conduction. *Upper right*, sagittal plane in complete right bundle branch block. *Lower left*, transverse plane in normal conduction. *Lower right*, transverse plane in complete right bundle branch block. Note that the conduction delay during the block is limited to the terminal portions of the loops.

permitted a unique opportunity to study the minute details in the change in intraventricular conduction. The sensitivity of the cathode ray oscilloscope permitted the careful distinction that the changes noted in the presence of complete right bundle branch block in this patient were clearly restricted to the terminal portion of the QRS spatial loop (Fig. 5). The earlier part of the ventricular excitation pathway remained unaltered regardless of whether or not right bundle branch block or normal intraventricular conduction was present. This is strong circumstantial evidence in support of the concept that the presence of right bundle branch block affects conduction only in the muscle area normally being excited last, and has little or no influence in the expected normal events of excitation in the early part of the QRS cycle. This again implies that septal activation, as well as the development of the major portions of the confluent intraventricular cones of excitation, occurs in the usual fashion in the presence of so-called right bundle branch block.

Comment: This young man with intermittent right bundle branch block did not demonstrate any underlying cardiac disease. One might raise the question of whether or not underlying myocarditis might not have precipitated the earlier manifestation of complete right bundle branch block. Nevertheless, there has been no clinical indication to suspect carditis for over a year, and there is relatively little clinical evidence to support the presence of myocarditis with the initial illness. The concept that the circulatory system would be embarrassed by such minor changes in cardiac rates at such a relatively low basal level is not considered very likely. The administration of 100 per cent oxygen had no influence upon conduction and, in fact, complete right bundle branch block persisted at the cardiac rate noted with oxygen inhalation. In the absence of demonstrable cardiac disease by either history or physical or laboratory examination other than the isolated finding of intermittent right bundle branch block, it was thought that this finding was insufficient evidence to justify the diagnosis of cardiac disease in an obviously robust, healthy, young person. He is cited as another example of intermittent complete right bundle branch

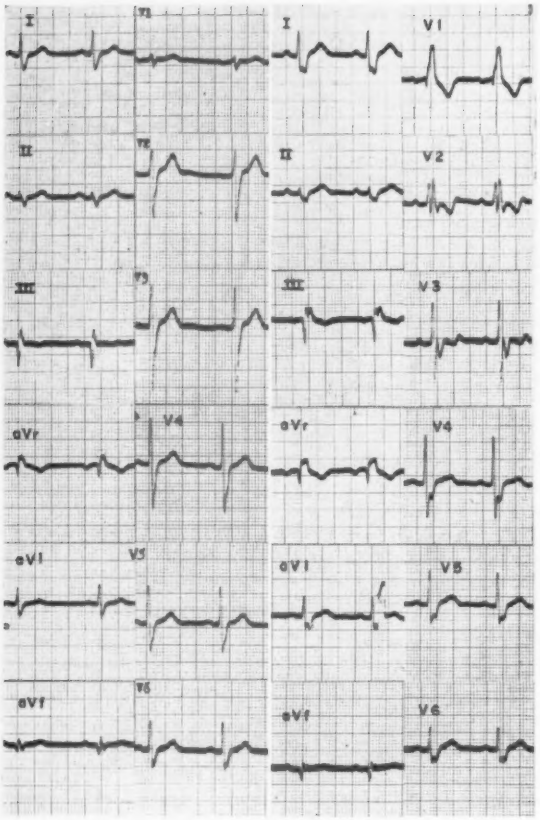

FIG. 6. Case 3. With an R-R interval of 0.88 second, intraventricular conduction defect is present (*left*) and with an R-R interval of 0.84 second or less complete right bundle branch block is obvious (*right*).

block associated with critical heart rates and not associated with apparent organic heart disease.

CASE 3. This thirty-six year old officer was found to have a right bundle branch block on a routine annual physical examination. This was the patient's first electrocardiogram. He stated that he was always in good health and denied any history referable to cardiac disease. There was no previous history of diphtheria, scarlet fever, rheumatic fever or other illnesses suggestive of myocarditis. He was physically active, played golf regularly and at times played as much as 45 holes without difficulty. He had been through multiple survival courses without symptomatology. His family history was significant only in that his father, at age fifty-seven, suffered a myocardial infarction. His social history revealed him to be a moderate smoker of one-half to one pack of cigarettes a day and his alcoholic intake was limited to an occasional social cocktail. He stated he had always been somewhat overweight and had a good appetite.

On physical examination, the patient was 5 feet, 10 inches tall, weighing 207 pounds. His blood pressure was 128/78 mm. Hg. The cardiac tones were of good quality without thrills or murmurs. There were no other significant findings.

Laboratory examination was as follows: hemogram, normal; urinalysis, normal; fasting blood sugar, 108 mg. per cent; blood cholesterol, 260 mg. per cent; phospholipids, 250 mg. per cent; lipoprotein S_f 0–12, 351 mg. per cent; S_f 12–20, 70 mg. per cent; S_f 20–400, 238 mg. per cent; Gofman atherogenic index, 89.

Pulmonary function studies were normal with a vital capacity of 4,925 cc. and maximal breathing capacity, 144 L. per minute. The timed vital capacity revealed: one second, 87 per cent; two seconds, 97 per cent; three seconds, 100 per cent.

Electrocardiographic examination: The routine electrocardiogram on this patient demonstrated an intraventricular conduction defect which approached bundle branch block (Figs. 6 and 7). There was a broad S wave in lead I and the total QRS duration in that lead approximated 0.10 second. The character of the S wave in lead I and the broad Q wave in lead III suggested the presence of an intraventricular conduction defect. Admittedly, the significance of the negative complex in leads III and aVF must be

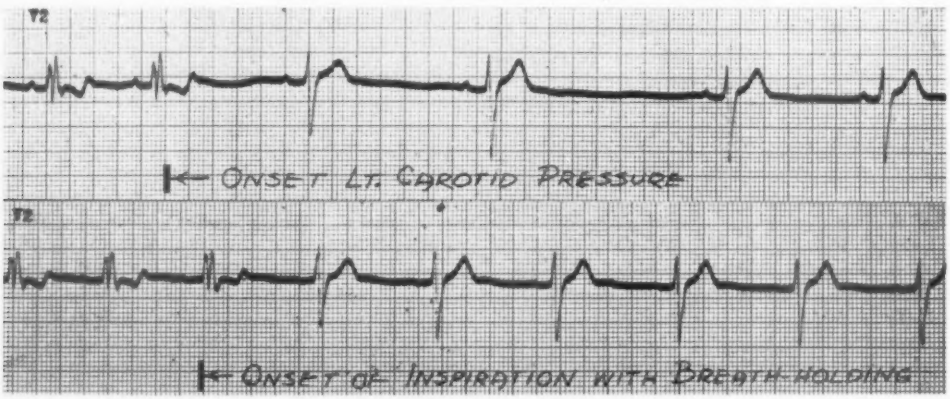

FIG. 7. Case 3. Demonstration of conversion of complete right bundle branch block to normal conduction with carotid sinus massage and with breath holding.

weighed in the light of clinical information. However, on the basis of the electrocardiogram alone, only the diagnosis of intraventricular conduction defect was thought to be justified.

It was soon ascertained that significant changes in the electrocardiogram could be induced by changes in the cardiac rate. With more rapid cardiac rates, the classic example of complete right bundle branch block was demonstrated (Fig. 6). There was further widening of the S wave in lead I and the development of the tall R′ complex in lead V_1. It is again interesting to note that the major changes in the electrocardiogram with the development of complete right bundle branch block were restricted to the terminal events of ventricular excitation. That conversion of intraventricular conduction defect to complete right bundle branch block was a critical function of cardiac rate was demonstrated by using carotid sinus massage, breath-holding technics, atropine administration and hyperventilation (Fig. 7).

Comment: Although this man is a more likely suspect for coronary artery disease due to his general obesity, there are a large number of people in the same category who do not warrant a clinical diagnosis of atherosclerotic heart disease. The only factual information pertinent to this case is the presence of an intraventricular conduction defect which can be converted to complete right bundle branch block as a function of critical heart rate. The amount of strenuous physical activity and general habitus of the individual concerned hardly suggests that he belongs to the group of subjects with impending cardiac death due to significant underlying heart disease.

Case 4. This thirty-nine year old American Indian was an Air Force officer. He was found to have an abnormal electrocardiogram at the time of his annual physical examination. This was the first electrocardiographic examination he had ever had. The only significant finding in his past history was a suggestion of labile hypertension. For over fifteen years, his blood pressure was noted to be elevated on first examination but returned to within normal limits after a short period of rest. In his past history, he recalled having had mumps in his teens but did not remember any other childhood diseases. He had no other significant past history. His father died at the age of thirty of tuberculosis, and one brother and one sister also had tuberculosis. His social history revealed that he smoked approximately one and a half packs of cigarettes a day and rarely indulged in alcoholic beverages.

Physical examination revealed a somewhat apprehensive man, 5 feet, 7 inches tall, weighing 150 pounds. His initial blood pressure was 165/108 mm. Hg.; a few minutes later, the blood pressure was recorded as 150/90. The fundi showed minimal hypertensive changes manifested by slight narrowing of the arterioles. No hemorrhages or exudates were noted.

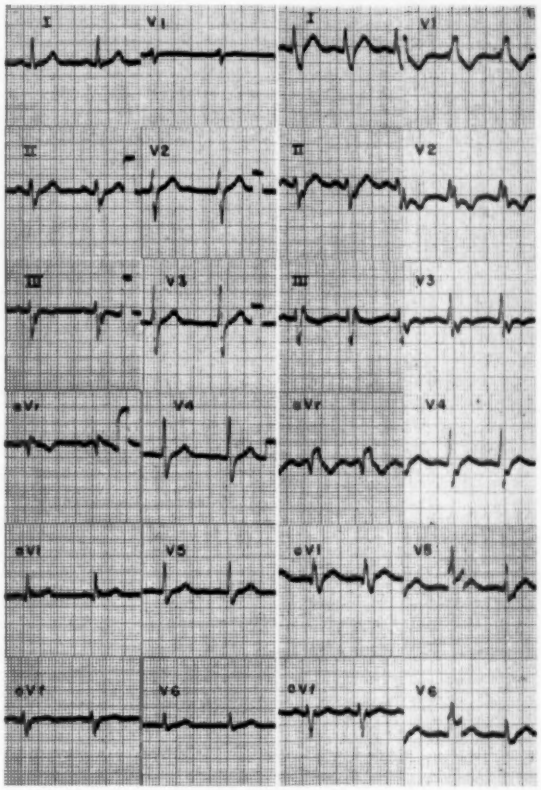

Fig. 8. Case 4. An intraventricular conduction defect is noted with an R-R interval of 0.68 second (*left*) and complete right bundle branch block with an R-R interval of 0.60 second (*right*).

Laboratory studies were as follows: hemogram, normal; urinalysis, normal; blood cholesterol, 212 mg. per cent; phospholipids, 230 mg. per cent; lipid studies S_f 0–12, 287; S_f 12–20, 40; S_f 20–400, 96; Gofman atherogenic index, 53; blood urea nitrogen, 10.5 mg. per cent; fasting blood sugar, 95 mg. per cent. A phenolsulfonphthalein test was within normal limits. The chest roentgenogram was normal.

The basic electrocardiogram showed a nonspecific intraventricular conduction defect (Figs. 8 and 9). The QRS duration was at the upper limit of normal with a broad splintered S wave in leads II, III and aVF. There was an initial splintered R wave in lead V_1. The interesting feature of this case was the demonstration of intermediate type complexes as a function of cardiac rate (Fig. 9). As in the previous cases, complete right bundle branch block was induced by increasing the cardiac rate. In this instance, the critical heart rate was approximately 100 per minute. In the other direction, a portion of the intraventricular conduction defect could be altered by further decreases in cardiac rate, and it was demonstrated that with a critical heart rate of approximately 55 per minute, there were significant changes in the

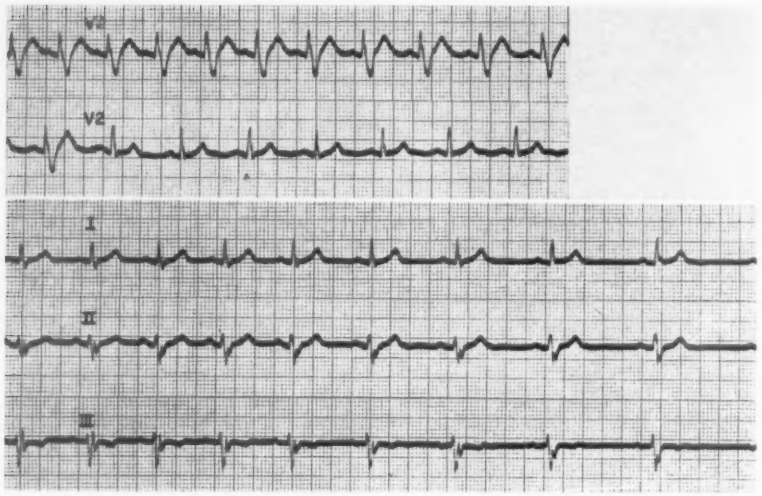

FIG. 9. Case 4. *Upper*, demonstration of intermittent character of complete right bundle branch block in V_2 as a function of cardiac rate. *Lower*, simultaneous leads I, II and III demonstrating disappearance of the terminal S wave in lead I and slight decrease in terminal time of activation with further cardiac slowing.

terminal portion of the QRS complex in leads I, II and III. In lead I, for example, the tiny terminal S wave actually disappeared. The duration of the S wave in leads II and III was decreased. This patient demonstrated two extremes in the presence of an intraventricular conduction defect; further normalization occurred with significant decreases in cardiac rate, while progression to complete right bundle branch block occurred with increases in cardiac rate.

Comment: During his evaluation, the patient's blood pressure readings fell to normal levels. With automatic blood pressure recording, the blood pressure over a period of three hours remained near 138/87 mm. Hg. It was thought that this patient presented the entity of an intraventricular condition defect which could be converted to complete right bundle branch block, as well as clinical manifestations of a vascular hyper-reactor. The changes in intraventricular conduction were obviously related to the cardiac rate. In the presence of relatively normal lipid profiles, cholesterol and phospholipid ratios, and in the absence of other significant history relative to coronary artery disease, it is difficult to establish the presence of underlying myocardial disease in this man. He presents the fourth example of intermittent complete right bundle branch block in a person forty years of age without sufficient evidence to warrant the clinical diagnosis of underlying heart disease.

CASE 5. This seventy year old man with epigastric distress was seeking a civil service appointment. He was seen by a colleague.* He is presented to show the conversion of left bundle branch block to normal intraventricular conduction following the compensatory pause after ventricular premature contractions (Fig. 10).

Comment: This man is obviously in the age group to present with significant arteriosclerotic heart disease and is symptomatic. The QRS changes during the left bundle branch block involve the entire excitation period rather than being restricted to the terminal events.

CASE 6. This forty-six year old man had a previous known myocardial infarction and an abnormal electrocardiogram. He was experiencing anginal symptoms and a repeat electrocardiogram was taken. Complete left bundle branch block was present. Due to the nature of his symptomatology and the recent appearance of left bundle branch block, a presumptive diagnosis of myocardial infarction was made and the patient treated accordingly. A subsequent electrocardiogram demonstrated absence of left bundle branch block and the presence of abnormal T waves across the precordium. Recent records demonstrate persistant complete block (Fig. 11).

Comment: This is another example of intermittent complete left bundle branch block in the presence of underlying heart disease. As in Case 5, left bundle branch block demonstrated changes throughout the entire QRS complex.

COMMENTS

On reviewing the literature, one is struck

* Courtesy of Jay Nadel, M.D., Travis Air Force Base, California.

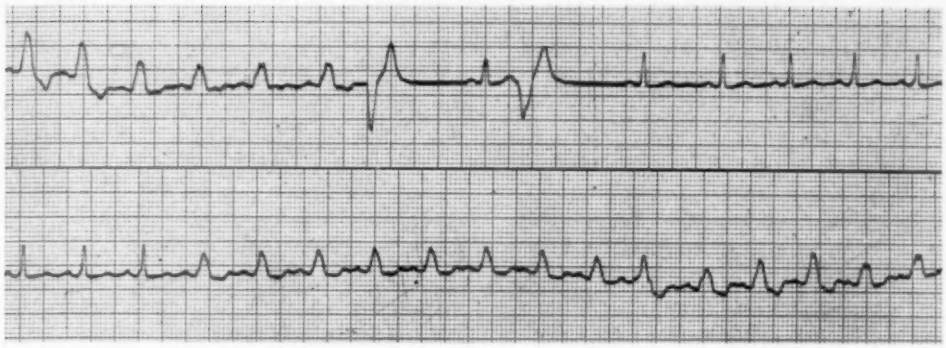

FIG. 10. Case 5. Demonstration of intermittent left bundle branch block. The compensatory pause following the ventricular premature contractions marks the onset of normal conduction.

with the prevailing opinion that intermittent bundle branch block is a sign of heart disease, and that a vast majority of the cases are of the left bundle branch block type. Comeau et al,[2] for example, in summarizing seventy-one cases of intermittent bundle branch block include only six examples of right bundle branch block. Other series[1] are limited to left bundle branch block alone. Nearly all series deal with patients presenting with recognized underlying cardiac disease, e.g., rheumatic heart disease with intermittent right bundle branch block. It is clear that either intermittent right or left bundle branch block may be associated with heart disease; however, the incidence reported in the literature is very heavily weighted to the side of intermittent left bundle branch block. These points may well have colored the initial impression that intermittent bundle branch block was a bad omen. The question is raised, "Is there a difference in intermittent right bundle branch block and intermittent left bundle branch block?"

In approaching the clinical significance of intermittent bundle branch block, it would be well to avoid the pitfalls that have plagued similar analysis of permanent right or left bundle branch block. Obviously, it is foolish to suppose that a mere long term follow-up of patients with a given finding proves it is not indicative of underlying cardiac malfunction. It is well known that many patients with recognized myocardial infarction have been followed for ten to twenty years without death. How then can a ten year follow-up of an individual with left bundle branch block warrant the opinion of "benign?" Knowing the incidence of coronary artery disease above the age of forty, what basis of fact permits the clinician to say that bundle branch block in such person is not a result of myocardial disease? While such long term evaluations help us to realize that such a finding in itself is not an ominous sign of impending death, they do not establish etiologic factors. Left bundle branch block secondary to coronary artery disease can hardly be considered "benign." Vesell[7] has already reported a ten year follow-up on a patient with intermit-

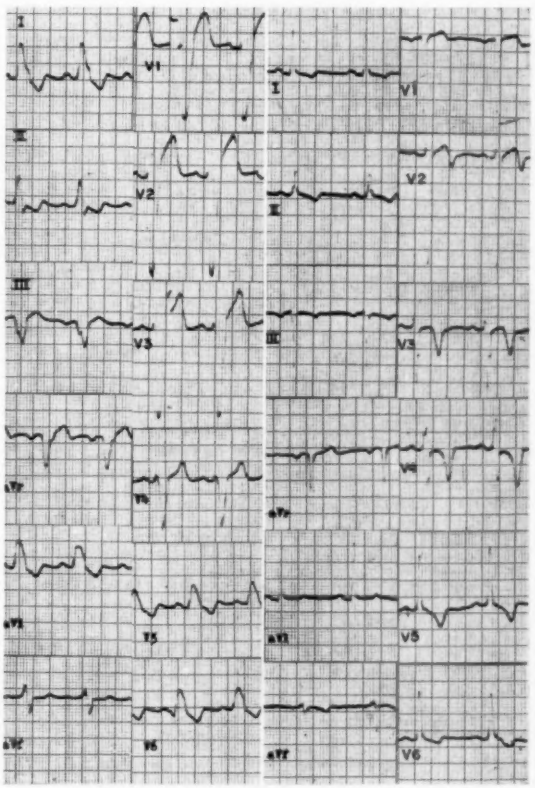

FIG. 11. Case 6. Complete left bundle branch block (*left*) and conversion to the normal order of excitation (*right*). The latter tracings show evidence of previous myocardial infarction.

tent bundle branch block and myocardial infarction. It follows, that like permanent bundle branch block, the prognosis in intermittent bundle branch block is dependent upon the severity of the underlying cause.

Another interesting facet of intermittent bundle branch block is the opportunity to evaluate the forces of ventricular excitation in normal and abnormal conduction. In all four cases of right bundle branch block in this series, the changes were restricted to the terminal portion of the QRS cycle. It follows that only the order of excitation through the last areas of activation is altered. The early events of excitation must continue in the same manner whether or not right bundle branch block exists. A survey of published records of intermittent right bundle branch block reveals a similar finding.

The terminal changes in the QRS complex which produce the broad terminal S wave in lead I and terminal broad R wave in V_1 are strongly suggestive of the aberration noted in premature atrial contractions. Berliner et al.[15] demonstrated that aberration in this instance was often related to the degree of prematurity of the premature beat or its encroachment upon the relative refractory period of the preceding cycle. Heart rate has long been recognized as a factor in intermittent bundle branch block whether or not one ascribes to direct control of the refractory state of the cardiac muscle by the vagus. According to most theories of ventricular excitation, it must be assumed that the septum begins activation very early in the QRS cycle. The stability of this period of the QRS complex hardly suggests a change in the order of normal septal activation. The spatial orientation and time of the change in excitation forces suggest that the area of muscle involved in the observed change in the order of activation is in reality the base of the heart or its septum. It has long been established that the base of the heart is the last portion of the ventricles to pass out of the refractory state. It is to be assumed then that this would also be the area of muscle most likely to be in a relative refractory state at the time of arrival of the new excitatory impulse.

Left bundle branch block appears to cause a complete reorientation from the normal sequence of ventricular excitation. The earliest portion of ventricular excitation is altered. Whether or not the difference in change in excitation in right and left bundle branch block is of clinical significance remains to be evaluated. On the surface it suggests that the abnormal Q waves of myocardial infarction may still be identified in some examples of infarction with right bundle branch block.

The demonstration of the important role of the critical heart rate in bundle branch block suggests extreme caution in assessing the role of oxygen inhalation or other measures in causing reversal of bundle branch block. The extremely narrow range of change in cardiac rate necessary to cause conduction changes hardly permits the interpretation of improved circulatory dynamics. The gradual change in the terminal QRS event with increasing cardiac rates seen in Case 4 suggests an increasingly larger area of heart muscle caught in the relative refractory phase of the preceding excitation cycle. What causes the relative refractory state to be prolonged in certain instances awaits further information. It seems certain from the cases reported herein and from a few other scattered case reports that it is not necessarily associated with significant underlying heart disease. One wonders how many cases of right bundle branch block might be induced by increasing the critical heart rate in individuals with such findings as S_1, S_2, S_3 pattern or delay in activation over the right ventricle. In any event, it is apparent that the underlying disorder is the important prognostic consideration. Perhaps more consideration should be given to the question as to whether or not right or left intermittent bundle branch block is present. Several instances are now available wherein intermittent right bundle branch block does not appear to be associated with discernible heart disease.

Summary

The pertinent literature on intermittent complete bundle branch block is critically reviewed. It is pointed out that the majority of cases reported are of intermittent left bundle branch block.

Four cases of intermittent complete right bundle branch block without apparent heart disease are reported. Critical heart rate appeared to be the dominant feature determining whether complete bundle branch block was present or not.

Vectorcardiograms during normal conduction and complete right bundle branch block demonstrated conclusively that the changes in

conduction were confined to the terminal QRS interval in contradistinction to the excitation in left bundle branch block.

The low incidence of intermittent complete right bundle branch block is apparent in that only the four reported cases were found in an electrocardiographic survey of approximately 70,000 asymptomatic subjects.

For comparison two cases of intermittent left bundle branch block in the presence of heart disease are included.

It is suggested that intermittent right bundle branch block may not have the same significance as intermittent left bundle branch block. Studies on intermittent right bundle branch block reveal fundamental information on the excitation process in complete right bundle branch block.

References

1. Shearn, M. A. and Rytand, D. A. Intermittent bundle branch block. *Arch. Int. Med.*, 91: 448, 1953.
2. Comeau, W. J., Hamilton, J. G. M. and White, P. D. Paroxysmal bundle branch block associated with heart disease. *Am. Heart J.*, 15: 276, 1938.
3. Lewis, T. An address on certain physical findings of myocardial involvement. *Brit. M. J.*, 1: 484, 1913.
4. Wilson, F. N. and Herrmann, G. R. Some unusual disturbances of the mechanism of the heart beat. *Arch. Int. Med.*, 31: 922, 1923.
5. Baker, B. M. The effect of cardiac rate and the inhalation of oxygen on transient bundle branch block. *Arch. Int. Med.*, 45: 814, 1930.
6. Vesell, H. Critical rates of ventricular conduction; unstable bundle branch block. *Am. J. M. Sc.*, 202: 198, 1941.
7. Vesell, H. and Friedfeld, L. Critical rates in ventricular conduction; duration of unstable bundle branch block. *Am. Heart J.*, 44: 830, 1952.
8. Lasser, R. P. and Grishman, A. Spatial vectorcardiography: Right bundle branch block. VIII. *Am. Heart J.*, 42: 513, 1951.
9. Gardberg, M. and Rosen, I. L. The cube vectorcardiogram in various degrees of right bundle branch block. *Am. J. Cardiol.*, 2: 572, 1958.
10. Digilio, V. A. Reversible bundle branch block in a case of toxic goiter. *Am. Heart J.*, 15: 116, 1938.
11. Kalett, J. Bundle branch block with spontaneous remission after four years. *Am. Heart J.*, 29: 120, 1945.
12. Boyadjian, N. and van Dooren, F. Raccourcissement des complexes QRS dans les blocs intraventriculaires suite aux modifications du rythme. *Acta cardiol.*, 6: 254, 1951.
13. Sandberg, A. A., Wener, J., Master, A. M. and Scherlis, L. Intermittent and transient bundle branch block: A clinical and electrocardiographic study. *Ann. Int. Med.*, 35: 1085, 1951.
14. Nichols, E. Transient right bundle branch block; wide S wave type in which normal conduction occurred both spontaneously and in response to vagal stimulation. *Ann. Int. Med.*, 30: 196, 1949.
15. Berliner, K. and Lewithin, L. P. Auricular premature systole; aberration of the ventricular complex in the electrocardiogram. *Am. Heart J.* 29: 449, 1945.

Suppressive Effect of Carotid Sinus Stimulation on Premature Ventricular Beats in Certain Instances*

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It is a generally accepted fact that carotid sinus stimulation will frequently induce ventricular arrhythmias, the commonest of which are premature beats. That the same type of stimulation may at times also suppress such ectopic activity of the ventricles seems to be denied by many physiologists and cardiologists. In their extensive monograph, Scherf and Schott[1] recognize that such a suppressive effect does occur and refer to the work of Wenckebach and Winterberg[2] relative to ventricular tachycardia and to the papers of Kleemann,[3] and Kaufmann and Rothberger[4] concerning ventricular extrasystoles. Kleemann alludes to several cases, while Kaufmann and Rothberger describe a single instance in which "vagus" pressure caused the disappearance of the extrasystoles; electrocardiograms are not reproduced in either paper. Regniers[5] produced premature ventricular beats by decreasing carotid sinus tension through carotid artery occlusion and then suppressed the ectopic beats with carotid sinus pressure; he refers to similar work by Kisch. In a case of parasystole, Eckey[6] produced a slowing of the rate of the ectopic beats by carotid sinus pressure. Golbey et al.[7] reported on one instance of parasystole in which there was a progressive lengthening of the interectopic intervals during carotid sinus pressure and on a second patient in whom there was a change in form of the ectopic ventricular beats.

The present experiments were initiated through the previous study of a case of paroxysmal supraventricular tachycardia exhibiting abnormal complexes thought to be premature ventricular beats which were suppressed along with the supraventricular beats during carotid sinus stimulation. Although it was not decided definitely about the site of origin of the abnormal complexes in this case, sufficient interest was aroused to begin an investigation of other instances of more clear-cut examples of premature ventricular beats.

Patients chosen for study were those with premature ventricular beats which were consistently numerous at a time when electrocardiographic control was possible. Combined pressure and massage were applied to one carotid sinus, starting with the side most conveniently accessible.

A suppressive effect on the premature beats was considered to be present when carotid sinus stimulation caused a disappearance or a decrease in the relative number of ectopic beats on repeated trials. In all, there were found eight patients who manifested this type of response, and these form the basis for this report. Several other instances of isolated responses were found, but since the results were not repeatedly or consistently reproduced, these cases were rejected.

Case Reports

Case 1. H. K., a forty-three year old white man, gave a history of palpitation and irregular heart action on and off for the past fifteen years. He was quite nervous and apprehensive. When examined on February 23, 1950, no evidence of heart disease was found, but there were numerous premature ventricular beats. Carotid sinus pressure caused transient faintness and cessation of the premature beats.

On April 7, 1954, he was again seen with the same arrhythmia. During runs of the premature beats, left carotid pressure was associated with disappearance of the abnormal beats (Fig. 1A).

Case 2. A. R., a sixty-six year old white woman, was referred on May 20, 1950, because of pressure

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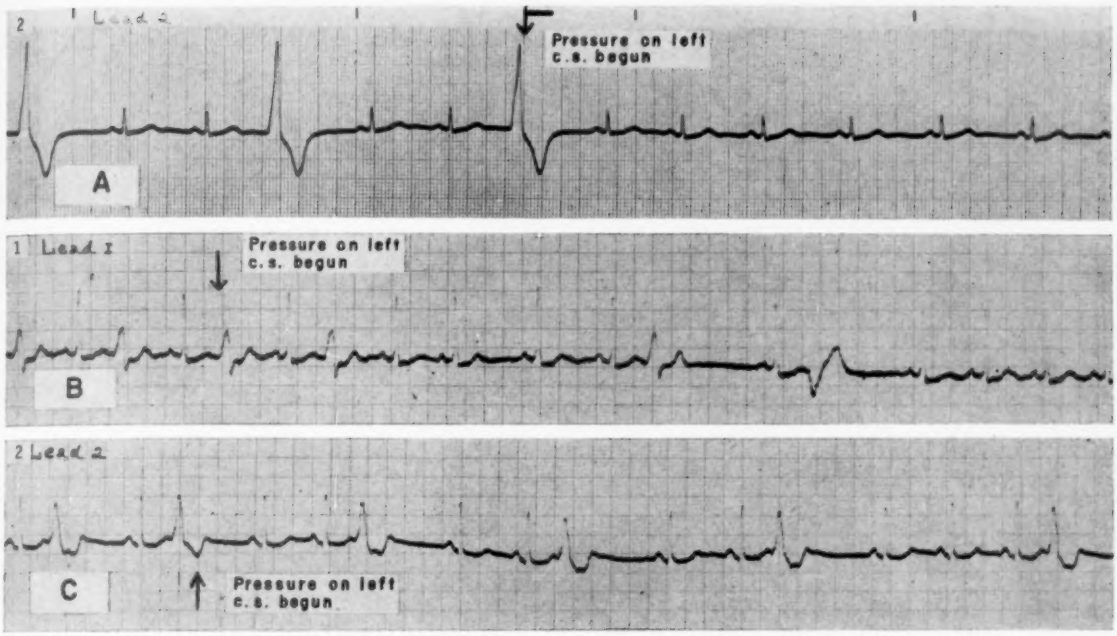

FIG. 1. A, Case 1. Lead II. Complete disappearance of premature ventricular beats occurs on left carotid sinus pressure. B, Case 2. Lead I. On left carotid sinus pressure bigeminy is replaced by less frequent premature beats, one of which arises in a different focus. C, Case 3. Lead II. Again bigeminy is interrupted by a slower ectopic rate. Carotid sinus pressure was maintained throughout the latter portion of each record.

sensations in the left side of the chest and irregular heart action for the past two weeks. She had had a thyroidectomy in 1945 and since then had taken thyroid extract fairly regularly; recently, because of increasing fatigue, she had tripled her thyroid dosage. Moderate fluctuating hypertension had been present for twenty years.

Examination revealed a moderately enlarged heart, a grade 2 systolic murmur over most of the precordium, and very numerous premature ventricular beats, usually producing bigeminy. Ventricular rate was 110 per minute. Pressure on either carotid sinus was invariably followed by a reduction or disappearance of the premature beats. One instance in which bigeminy was interrupted is shown in Figure 1B. Thyroid medication was stopped and during the next several months ectopic beats were infrequent.

On June 18, 1951, the patient had an anterior myocardial infarction with an uneventful recovery. On August 27, 1951, she was again observed with numerous premature ventricular beats (every second or third beat). The electrocardiographic pattern of the premature beats was quite similar but not identical with the pattern of those on May 20, 1950. The total ventricular rate at this time was 75 per minute. Pressure on either carotid sinus resulted in some slowing of the ventricular rate and a slight increase in the intervals between the premature beats but no decrease in their relative number.

CASE 3. C. B., a fifty-eight year old white woman, was seen on October 8, 1951, complaining of pressure feelings in the chest and irregular heart action off and on for several months. There was also paresthesia of the hands and feet at times. No abnormality of the heart was found except for frequent premature ventricular beats, usually every second but occasionally every third beat. Pressure on either carotid sinus was followed by a decrease in the relative and absolute number of premature beats (Fig. 1C). Although this reduction was not striking, it occurred consistently. Shortly after releasing carotid sinus pressure the premature beats would invariably become numerous again.

CASE 4. J. B., a forty-five year old white man, was first seen on November 14, 1951. He complained of a "nervous feeling" in the chest and abdomen. Palpitation had been a symptom off and on since childhood; alcohol, tension and exertion were believed to be precipitating causes. There was no history of rheumatic fever or hypertension. Examination was essentially negative except for frequent premature ventricular beats, an occasional one being interpolated.

On this visit and a subsequent one, pressure on the left carotid sinus was consistently followed by either a marked reduction or complete disappearance of the premature beats. Three examples are shown in Figure 2. A minute or two after release of pressure the premature beats would again become numerous. The ventricular rate before carotid sinus pressure varied between 80 and 85 per minute; definite slowing, sometimes slight, occurred during pressure.

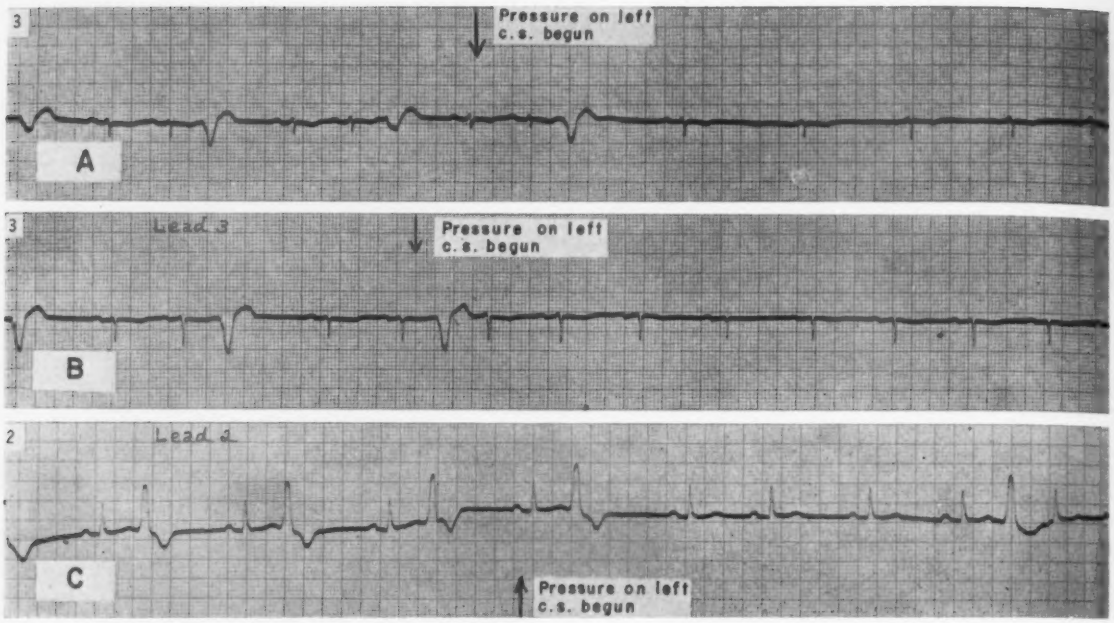

FIG. 2. Case 4. Three different experiments on the same patient. A and B were taken on one visit, C on another. One interpolated beat is seen in B just after carotid sinus pressure was begun and another in C near its end. Carotid sinus pressure was maintained throughout each record to the right of the arrow.

CASE 5. D. H., a thirty-eight year old white woman, was referred for cardiac studies on August 21, 1954. She complained of nervousness and shooting pains in the left side of the chest. There was no history of rheumatic fever or hypertension. Examination was essentially negative except for numerous ventricular beats (usually every third beat). Approximately four seconds after initiating left carotid sinus pressure the premature beats disappeared (Fig. 3A) and did not return immediately after release of pressure. The experiment was repeated with almost identical results.

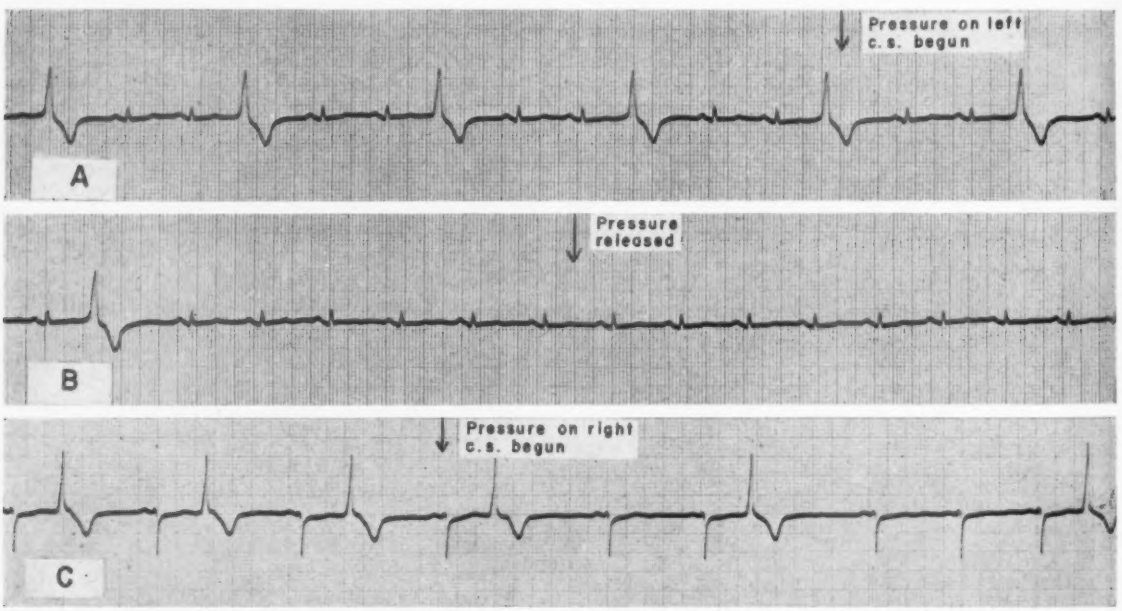

FIG. 3. A and B are continuous tracings from Case 5 (Lead III). The premature beats do not return immediately after carotid sinus pressure is released. C, Case 6 (Lead III). Bigeminy ceases shortly after right carotid sinus stimulation; pressure on the left side in this case had no effect on the premature beats.

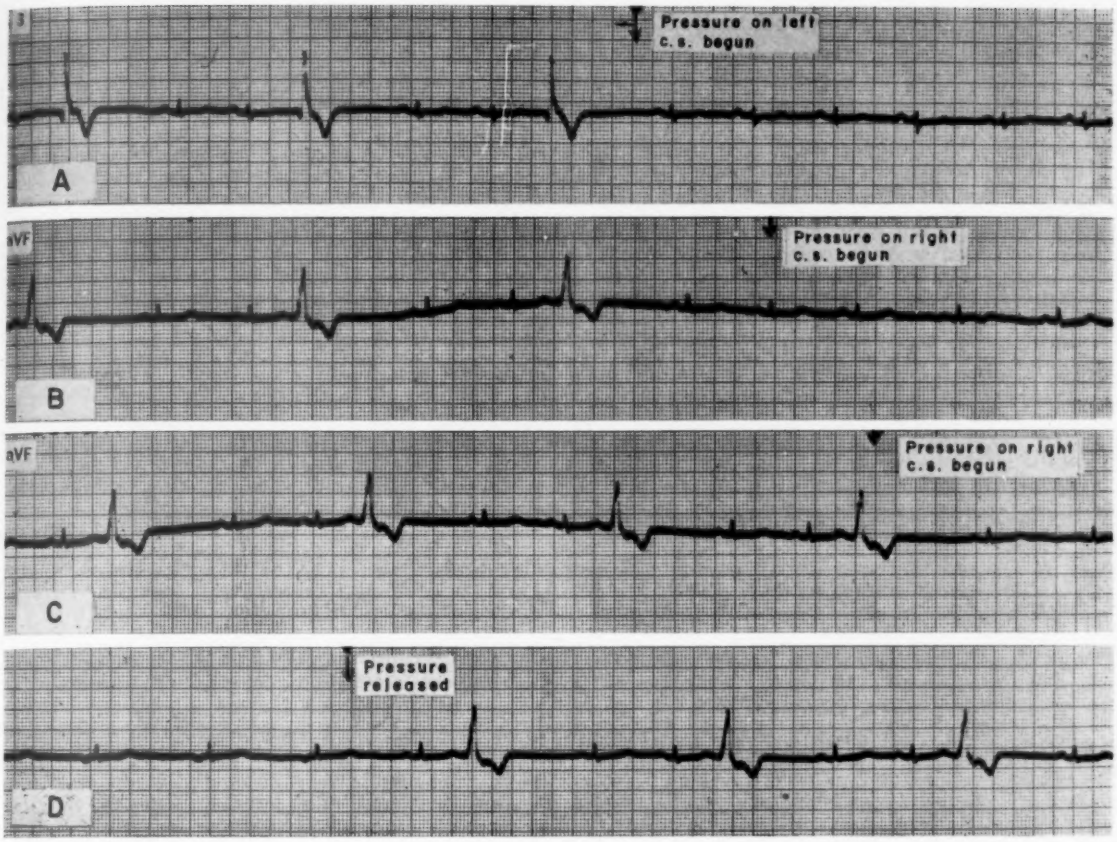

FIG. 4. A, Case 7. Complete disappearance of premature beats on one of the trials in this patient. B, C and D are from Case 8. In B is shown one of the few examples in which suppression of the ectopic beats occurred before any slowing of the heart rate. C and D are continuous and demonstrate an immediate return of the premature beats after release of carotid sinus pressure.

CASE 6. E. S., a seventy-eight year old Negro woman, was seen on September 17, 1954. She complained of high epigastric distress and nausea following meals and frequent spells of nervousness. Examination revealed mild hypertension and numerous premature ventricular beats with long runs of bigeminy. Repeated pressure on the right carotid sinus always caused a decrease in the number of premature beats (Fig. 3B). Pressure on the left side was without effect.

CASE 7. A. B., a thirty year old Negro woman, complained of a constant pain in the left chest. There was no dyspnea or anginal type of pain. A grade 1 systolic murmur was present at the apex. Fluoroscopy of the chest was negative. The electrocardiogram was normal except for premature ventricular beats occurring every third beat. The ventricular rate was 76 per minute. Pressure on either carotid sinus caused prompt disappearance of the premature beats with slight slowing of the total rate (Fig. 4A).

CASE 8. A. A., a fifty-six year old white woman, had noticed irregular heart action for some time. Otherwise there was no evidence of cardiac abnormality. The ventricular rate was about 72 per minute, premature ventricular beats occurring every third beat. Pressure on either carotid sinus resulted in immediate cessation of the ectopic beats, the latter usually recurring promptly after release of pressure (Figs. 4B, C and D).

COMMENTS

It is seen that five of the eight subjects had no evidence whatsoever of heart disease and only one (Case 2) had any serious disease. This latter patient is of particular interest because on the initial visit, while on excessive thyroid medication, yet without definite symptoms of angina or congestive failure, her premature beats were suppressed by carotid sinus pressure, but on a subsequent date, following a myocardial infarction and with a slower ventricular rate, carotid sinus stimulation was without effect on the ectopic beats; since the patterns of the premature complexes were quite similar on both visits, one might assume that the sites of origin were at least nearby on the two occasions.

In Cases 1 and 4 the patients were also subjected to carotid sinus pressure on two different visits; unlike Case 2 these patients responded with a suppression of the premature beats during both trial periods. In four (Cases 2, 6, 7 and 8) of the eight patients pressure was applied to both sides (separately). In three of these the effect was similar on either side. In one (Case 6) there was suppression of the ectopic beats on right carotid sinus pressure but no inhibition on repeated left-sided stimulation. In the latter instance, however, none of the usual effects of carotid sinus pressure, such as slowing of the sinus rate, was produced; hence, it seems likely that sensitive nerve endings were not stimulated on the left side.

There was no instance of parasystole encountered during these experiments. Occasionally a slight variation in the coupled interval was noted, particularly after carotid sinus pressure.

The incidence of a suppressive response on premature ventricular beats by carotid sinus stimulation was not determined in this study, but the impression was gained that the frequency was low in those with organic heart disease and in overdigitalized patients and high in persons without evidence of heart disease. This impression brings to mind the prediction by Hering[8] that carotid sinus pressure might be useful in differentiating extrasystoles due to nervous influences and those resulting from organic heart disease, though this author does not specifically mention ventricular extrasystoles.

Slowing of the ventricular rate accompanied (or rarely followed) the suppression of ectopic ventricular beats in all instances. In some experiments this slowing was considerable; in others it was minimal. After release of carotid sinus pressure the time interval for return of the premature beats to their previous frequency varied markedly. Rarely, their return was almost immediate (Fig. 4D); more often it was delayed, at times up to a minute or longer.

POSSIBLE MECHANISMS INVOLVED

The mechanism by which the premature ventricular beats were suppressed in these cases cannot be definitely ascertained from the present data, but a number of possibilities come to mind. These may be grouped into *indirect* and *direct effects* resulting from stimulation of the vagus and sympathetic nerves.

Indirect Effects: The carotid sinus reflex is broad and complex. Conceivably, any of its effects, such as changes in blood pressure or respiration, might influence the number of premature ventricular beats. However, only the possible relationship with heart rate will be discussed here.

As stated above there was a simultaneous slowing of the supraventricular rhythm in nearly all instances. In fixed coupled rhythms such as in the present cases one might well expect that a change in the dominant rhythm would alter the ectopic one. The experiments of Goldenberg and Rothberger[9] and Scherf[10] support this view to some extent. After producing regularly occurring ventricular extrasystoles in dogs, these investigators stimulated the vagus nerve and induced cardiac standstill; not only did the ventricular extrasystoles disappear during the prolonged period of asystole but they also failed to reappear immediately when cardiac activity was resumed. Since the vagus does not innervate the ventricles, the dependence of the extrasystole on an initiating beat was demonstrated. Furthermore, a delayed effect on the excitability of the ventricular focus was suggested.

In the cases herein reported, one might postulate that the premature beats depend upon a change in excitability of the ventricle produced by the supraventricular beats and that this change is related to supernormality following each beat. It could be assumed that, other factors being the same, the faster the heart beats the greater would be the supernormality after each beat. On the contrary, slowing the heart would reduce supernormality and tend to reduce the likelihood of ventricular premature beats during this period.[11]

However, there are a number of arguments against the latter theory and against the slowing of the heart rate *per se* as the causative factor. Siebens et al.,[12] working with the dog's ventricle, failed to alter consistently the amplitude of supernormality by changes in rate. Also, it seems to be generally accepted by clinicians that a slow rate predisposes to premature ventricular beats in the normal heart. Actually, however, information on this point is rather sparse. Exercise, which brings in other factors besides rate, has variable effects; most often there is a decrease in the ectopic beats in normal persons and an increase in those with coronary disease.[14] Quite similar responses have been noted following the increase in rate after the administration of amyl nitrite.[15] And finally, in an occasional

instance (too rare to be more than suggestive) during the present investigation, the premature beats ceased before the supraventricular rate was changed (Fig. 4B).

Direct Action: It is generally accepted that fibers of the vagus do not extend to the human ventricular musculature, though opinions to the contrary can be found.[15] All agree, however, that the vagus does supply the A-V node and A-V bundle. A remote possibility is that the ectopic beats in the present cases arose in the A-V node or bundle, and aberrant ventricular conduction produced the abnormal complexes. Might the vagal impulses to the bundle also be transmitted into its branches? If so, then ectopic beats arising in the bundle branches might be influenced directly by the vagus.

It is agreed that fibers of the sympathetic nerves are distributed directly to the ventricular muscles. Stimulation of the accelerans, particularly when combined with various drugs or simultaneous vagal stimulation, has precipitated premature ventricular beats in animals.[1] It therefore seems possible that an increase in the normal sympathetic tone would also result in these ectopic beats. If so, then a decrease in an elevated tone would be expected to suppress the premature contractions. By increasing the pressure within the carotid sinuses of cats, Bronk, Ferguson and Solandt[16] caused a decrease or disappearance of impulses along the cardiac accelerators. If the same reaction occurs in man, then a satisfactory explanation for the suppression of premature ventricular beats by carotid sinus pressure is thereby offered.[1]

The striking relief of pain by carotid sinus stimulation in many instances of angina pectoris comes immediately to mind during such a discussion. The mechanism of pain relief is not yet clear, but the work of Freedberg and Riseman[17] indicates that slowing of the heart rate is not an important factor. These investigators felt that pain was relieved through an interruption of afferent impulses along sympathetic reflex arcs; however, such a conclusion does not seem to be based upon proved physiologic principles. Vasodilation was considered to be unlikely by these authors particularly because of differences between the reaction to nitroglycerin and the carotid sinus response. Could an inhibition of the efferent impulses and the resulting decrease in muscular tone be involved in this phenomenon?

It may be significant that in all of the present eight patients there was some evidence of nervous imbalance, and the heart rate tended to be fairly rapid at the time that carotid sinus pressure was effective. This would point to the probability of an increase in sympathetic tone at such times; and, by removal of this hypertonicity, carotid sinus pressure may well have suppressed the premature beats. However, the rapidity of the response in most instances argues against a pure sympathetic action; also the scanty knowledge concerning the effects of efferent sympathetic impulses on the human ventricle should make one cautious in arriving at definite conclusions on this question.

Summary

Suppression of premature ventricular beats by carotid sinus stimulation was repeatedly induced in eight individuals. Slowing of the heart rate accompanied or followed this suppression in all instances. The majority of these cases showed no evidence of heart disease.

The mechanism of suppression by the carotid sinus reflex is not made apparent by the present data, but several possibilities are proposed. These are divided into indirect effects, the chief of which is a change in supernormality of the ventricular muscle resulting from slowing of the heart rate, and direct effects, by way of the vagus and sympathetic nerves.

References

1. Scherf, D. and Schott, A. Extrasystoles and Allied Arrhythmias. New York, 1953. Grune & Stratton.
2. Wenckebach, K. F. and Winterberg, H. Die unregelmassige Herztatigkeit. Leipzig, 1927. Engelmann.
3. Kleemann, M. Der Vagusdruckversuch und seine Bedeutung fur die Herzfunktion. *Deutsches Arch. klin. Med.*, 130: 221, 1919.
4. Kaufmann, R. and Rothberger, C. J. Beitrage zur Entstehungsweise extrasystolischer Allorhythmien. 3. Mitteilung. *Ztschr. ges. exper. Med.*, 9: 104, 1919.
5. Regniers, P. Le sinus carotidien en clinique. *Rev. Belge sci. méd.*, 2: 601, 1930.
6. Eckey, P. Untersuchungen uber autonome Nervenwirkungen auf die Herzkammern des Menschen. *Arch. Kreislaufforsch.*, 5: 1, 1939.
7. Golbey, M., Ladopulos, C. P., Roth, F. H. and Scherf, D. Changes of ventricular impulse formation during carotid pressure in man. *Circulation*, 10: 735, 1954.
8. Hering, H. E. Uber das Auslosen oder Beseitigen heterotoper Herzschlage beim Karotisdruckversuch. *Wien. Arch. inn. Med.*, 10: 497, 1925.
9. Goldenberg, M. and Rothberger, C. J. Experimentelle Beitrage zur Kenntnis der Strophantin-Extrasystolen. *Ztschr. ges. exper. Med.*, 79: 705, 1931.
10. Scherf, D. Experimental digitalis and strophan-

thin extrasystoles. *Exper. Med. & Surg.*, 2: 70, 1944.
11. Hoff, H. E. Personal communication, 1954.
12. Siebens, A. A., Hoffman, B. F., Gilbert, J. L. and Suckling, E. E. Effect of rate on excitability of dog's ventricle. *Am. J. Physiol.*, 166:610, 1951.
13. Mann, R. H. and Burchell, H. B. Premature ventricular contractions and exercise. *Proc. Staff Meet. Mayo Clin.*, 27: 383, 1952.
14. Bourne, G. An attempt at the clinical classification of premature ventricular beats. *Quart. J. Med.*, 20: 219, 1927.
15. Mitchell, G. A. G. Cardiovascular Innervation. Edinburgh, 1956. E. & S. Livingstone.
16. Bronk, D. W., Ferguson, L. K. and Solandt, D. Y. Inhibition of cardiac accelerator impulses by the carotid sinus. *Proc. Soc. Exper. Biol. & Med.*, 31: 579, 1934.
17. Freedberg, A. S. and Riseman, J. E. F. Observations on the carotid sinus reflex and angina pectoris. *Circulation*, 7: 58, 1953.

Studies of WPW Syndrome

Wolff-Parkinson-White Syndrome

A Vectorcardiographic, Electrocardiographic and Clinical Study*

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In 1915 Wilson described an electrocardiogram that demonstrated a short P-R interval and a wide QRS complex.[1] Wedd[2] in 1921 first called attention to the occurrence of paroxysmal tachycardia in a patient whose electrocardiogram showed a short P-R interval and wide QRS complex. However, it was not until 1930 that Wolff, Parkinson and White[3] published the first paper which described the clinical as well as the electrocardiographic findings in this syndrome.

Holzmann and Scherf[4] and Wolferth and Wood[5] postulated the bundle of Kent theory. They demonstrated anomalous atrioventricular muscular bundles, similar to those described by Kent many years earlier, in patients who exhibited this syndrome during life and who later came to autopsy. The shortened A-V conduction time was explained by the preferential conduction through the anomalous bundle and avoidance of the normal delay at the A-V node. This theory received further support from the ingeniously contrived experiments of Butterworth and Poindexter.[6] These investigators created an electrical atrioventricular communication. Sinoatrial node action potentials were amplified by the use of a vacuum tube amplifier, and an electrical circuit bypassing the atrioventricular node stimulated the left or right ventricle ahead of the normal spread of excitation. The electrocardiograms that were reproduced simulated those seen in man. Supraventricular tachycardia was produced by reversing the polarity of the system and sending ventricular action potentials back to the atria.

Segers, Lequime and Denolin[7] proposed that the delta wave or the deformity of the P-R interval was due to a supplementary action potential of the accessory muscle bundle responsible for the shortened A-V conduction. The concept of a fusion beat was introduced by Hunter, Papp and Parkinson.[8] They proposed that the atrial activity mechanically or electrically discharged an ectopic focus in the ventricle.

In 1945 Rosenbaum et al.[9] reviewed this subject and added their own observations on the characteristics of the precordial leads in patients with this syndrome. However, since that time, many investigators have studied patients with this syndrome utilizing newer technics such as intracardiac electrocardiograms[10,11] and simultaneous electrocardiograms recorded at different areas of the ventricles, and have experimentally reproduced electrocardiograms similar to those seen in man.[10,12] In addition, hemodynamic[13] and kymographic studies[14,15] have shed light on myocardial function in this syndrome.

Sodi-Pallares and his associates[10b] and Prinzmetal et al.[12] agree that the QRS complex is basically a fusion beat, but differ as to the manner by which this is brought about. Based on experiments in which complexes resembling WPW configurations were produced in dogs

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and on intracardiac electrocardiography in six patients with this syndrome, Sodi-Pallares et al. concluded that there were two areas on the right side of the interventricular septum that are hyperexcitable and respond to the mechanical contraction of the atrium or to weak atrial action potentials ordinarily too distant to be effective. This prematurely excites the right ventricle and hence they proposed the term "pre-excitation." In addition, they believe that part or all of the left ventricle is activated in a perfectly normal fashion via impulses that traverse the A-V node, common bundle and left bundle branches.

Prinzmetal and associates[12] proposed the theory of accelerated conduction. This was based on a series of experiments in which various types of electrical and mechanical stimuli were applied to different portions of the right ventricle, septum and tricuspid valve region of dogs. QRS complexes were produced that had a similarity to those seen in the WPW syndrome. However, when the bundle of His was cut, WPW-like complexes could no longer be produced by the previously successful methods. They therefore concluded that the A-V node and the bundle of His must be functioning for the WPW syndrome to occur. Furthermore, cinematographic studies were reported to show that a portion of the right ventricle contracts prematurely, indicating to these investigators that conduction must be accelerated in the node in order to stimulate the right ventricle ahead of the normal spread of excitation. They concluded, like Sodi-Pallares, that the spread of excitation of the left ventricle occurs in a normal manner.

Grishman and associates,[11] using simultaneous intracardiac, esophageal and extremity or chest leads, studied seven patients with this syndrome. Their findings suggested that the abnormal conducting mechanism carries the excitation wave simultaneously to portions of the posterior surface of the left ventricle and anterior surface of the right ventricle, and that the spread of excitation in the right ventricle is from the epicardium towards the endocardium. A complete functional block of the atrioventricular node occurs when conduction of the excitation wave follows the accessory pathways.

Grant et al.,[16] using the vector translating method, studied patients with the WPW syndrome during anomalous and then during normal conduction. The delta loop was formed by plotting instantaneous vectors derived from the normal loop and applying them to the loop obtained during WPW conduction. By drawing a line through the origin of these translated vectors a loop is formed which was considered to be the delta loop. It was small in one-half of the cases, but when it was large the authors concluded that a conduction defect must be present so that the method was not applicable to these cases. They found the delta vector parallel to the frontal plane of the body in 90 per cent of their cases, and concluded that the practice of dividing the cases into types A and B based on the configuration of the delta wave in lead V_1 depended upon a trivial difference in the direction of the delta vector.

There have been but a few reports describing the vectorcardiogram in this syndrome.[17–22] This paper presents the vectorcardiograms in thirty-eight cases. We reviewed our findings to see whether the vector supported one of the previously described theories. The vectorcardiographic correlation with the electrocardiogram, difficulties encountered in the diagnosis of myocardial infarction and ventricular hypertrophy in the presence of this syndrome, and the change in the vectorcardiogram and electrocardiogram when normal conduction is established will be presented.

Methods and Material

The material is comprised of thirty-four patients from the wards and clinics of The Mount Sinai Hospital, and four patients from the private practice of members of the Department of Cardiology. Thirty-six patients had the classic electrocardiographic criteria for the Wolff-Parkinson-White syndrome.[23] In two cases the P-R intervals of the electrocardiogram were longer than 0.12 second and these will be discussed separately.

The ages of the patients ranged from five to sixty-seven years. There were twenty-two males and sixteen females in the series. Four patients had congenital heart disease, including two cases of coarctation of the aorta, one of tetralogy of Fallot and one of tricuspid atresia. There were two patients who had rheumatic heart disease, one patient with arteriosclerotic heart disease and the remainder had no apparent heart disease. A history of palpitations was obtained in 50 per cent of the patients.

Vectorcardiograms were obtained with the cube method of electrode placement.[24] The Technicon cardiograph and vectorscope, or the Sanborn vector system and direct writing electrocardiograph were used in all cases. Simultaneous leads with higher amplification and double speed electrocardiograms were used in most cases.

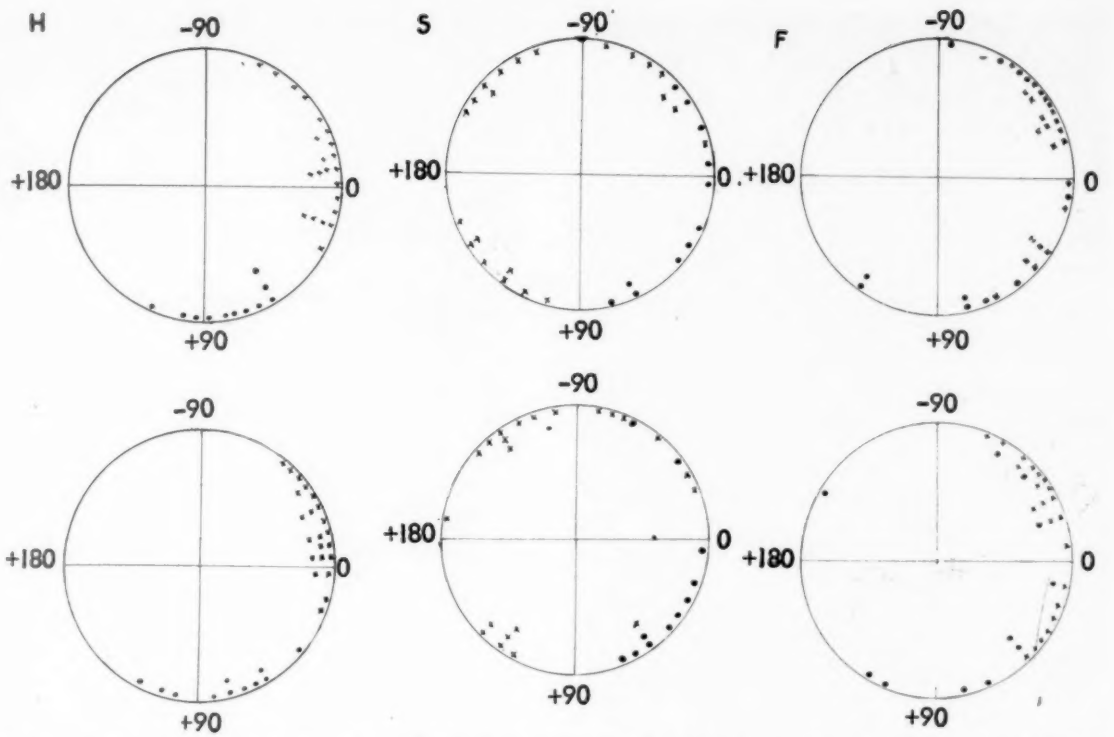

FIG. 1. ● = group A. × = group B. The spatial orientation of the delta wave (*above*) and delta plus QRS sÊ loop (*below*) is shown for all three planes in thirty-three patients. In the horizontal plane (H) the delta wave or the delta plus QRS sÊ loop is oriented between +30 degrees and +120 degrees in eleven patients (group A). In twenty-two patients the delta wave or the delta plus QRS sÊ loop is oriented between +30 degrees and −60 degrees (group B). In the sagittal plane (S) and frontal plane (F) no such separation into groups based on spatial orientation is feasible.

TERMINOLOGY

The terms "pre-excitation," "accelerated conduction," "anomalous excitation," "bundle of Kent syndrome" and many others have been used synonymously to describe the electrocardiographic features seen in the Wolff-Parkinson-White syndrome. Many of these terms imply a mechanism of ventricular excitation which remains unproved, consequently, we shall use the terms Wolff-Parkinson-White (WPW) conduction or the generic term, anomalous conduction, as not implying any specific mechanism throughout this paper.

RESULTS

Vectorially the cases were separated into two groups (Fig. 1) based on the orientation of the mean delta vector in the horizontal plane. Those in which the mean delta vector oriented anteriorly were classified as group A, and those in which the vector was oriented to the left (but also posteriorly or slightly anteriorly) were classified as group B. The delta wave is defined in the vectorcardiogram as the initial component of the QRS sÊ loop with the time markings slowly inscribed in contrast to the remainder of the loop. There was no difficulty encountered in determining the end of the delta wave and the onset of the remainder of the QRS sÊ loop. The electrocardiographic criteria for the diagnosis of the Wolff-Parkinson-White syndrome conformed to the criteria of Wolff.[23] The P-R interval is 0.12 second or less; the QRS duration 0.10 second or more, and there is a delta wave or slurred initial portion of the QRS complex noted in one or more of the leads.

GROUP A (ELEVEN CASES)

The Delta Wave: A delta wave was present in all eleven cases and could be seen in all three planes. It was directed anteriorly in all eleven and replaced the normal initial portion of the QRS sÊ loop ascribed to septal excitation (Fig. 2A). It was, in addition, oriented inferiorly in seven and superiorly in four.

QRS sÊ Loop—Horizontal Plane: The QRS sÊ loop was oriented anteriorly in all eleven and

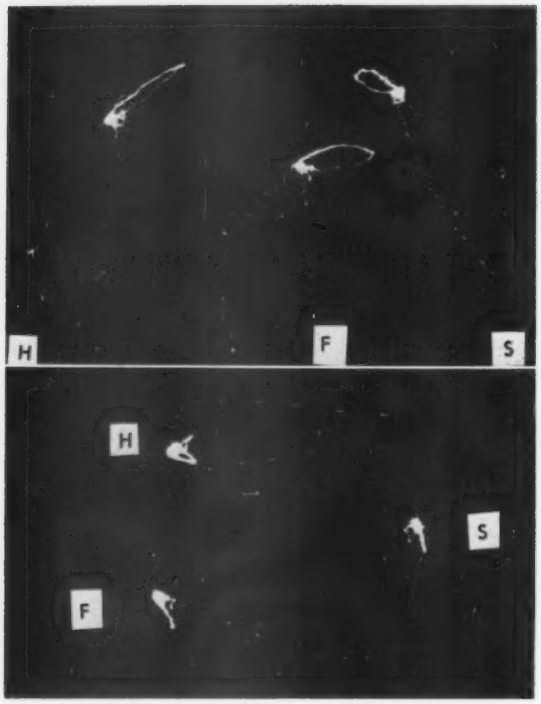

FIG. 2A. WPW syndrome, group A. *Top*, vectorcardiogram is oriented anteriorly, inferiorly, and to the right. Note the characteristic initial slow inscription (delta wave) of the QRS sÊ loop). *Bottom*, vectorcardiogram after conversion to normal conduction by quinidine. Note disappearance of delta wave and normal orientation of QRS sÊ loop in all planes.

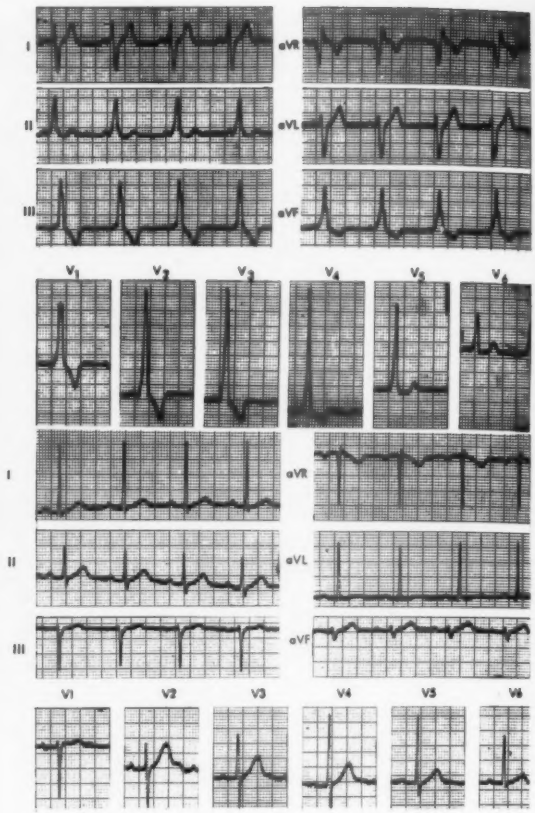

FIG. 2B. Corresponding electrocardiogram before and after conversion to normal conduction.

was always more than +30 degrees anterior to the horizontal axis (Fig. 2A). In eight patients it was between +30 degrees and +90 degrees, and in three it was between +90 degrees and +120 degrees. The direction of inscription of the QRS sÊ loop was a figure of eight in eight, counterclockwise in two, and clockwise in one.

QRS sÊ Loop—Sagittal Plane: In the sagittal plane the QRS sÊ loop was anteriorly oriented in all eleven cases. It was in addition, inferior in eight, superior in two, and inferior and then superior in one. The direction of inscription of the loop was clockwise in five cases, counterclockwise in four, and figure of eight in two.

QRS sÊ Loop—Frontal Plane: In the frontal plane the QRS sÊ loop was oriented to the left in nine cases and to the right in two. As in the sagittal plane the QRS sÊ loop was oriented superiorly in two, inferiorly in eight and inferiorly and then superiorly in one. The direction of inscription of the QRS sÊ loop was counterclockwise in five cases, clockwise in four, and figure of eight in two.

The T sÊ Loop: The T sÊ loop was discordant or at an angular deviation of greater than 60 degrees from the QRS sÊ loop in at least two of the three planes in eight cases. The T sÊ loop was concordant in all planes in one and concordant in two planes in two.

Group A Electrocardiogram: The P-R interval ranged from 0.09 to 0.12 second. The width of the QRS complex ranged from 0.10 to 0.18 second. A delta wave was present in every case (Fig. 2B). There were depressions of the S-T segment of 1 mm. or more in at least one of the precordial leads in nine, and in at least one of the extremity leads in seven cases. There were S-T segment elevations of 1 mm. or more in at least one of the extremity leads in five. The T waves were diphasic or abnormally inverted in one or more of the extremity and precordial leads in nine cases, and normal in all leads in only two. In four cases there were QS complexes in leads III and aVF, but in only one was there a Q wave in lead II. There was left axis deviation in five cases, right axis

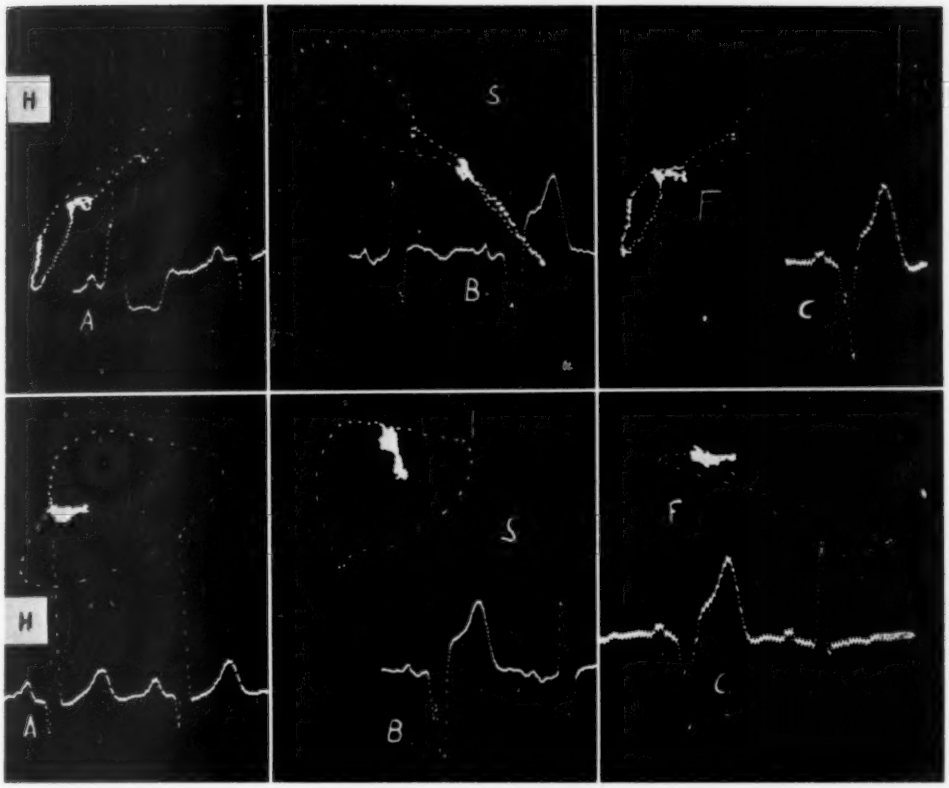

FIG. 3A. WPW syndrome, group B. *Top*, vectorcardiogram is oriented posteriorly, superiorly and to the left. The component leads A, B and C are inscribed with each vector loop. Note the initial slow inscription (delta wave) of the QRS sÊ loop. *Bottom*, the vectorcardiogram of every alternate beat which is normally conducted.

deviation in two cases and a normal axis in four cases.

Correlation of the Electrocardiogram and Vectorcardiogram: There were tall R waves with no S waves in the right precordial leads (Fig. 2B) which correlated with the all anterior orientation of the QRS sÊ loop in the horizontal plane. Q waves or QS complexes in leads III and aVF of the electrocardiograms were noted in the cases in which the delta wave of the vectorcardiogram was initially oriented superiorly. Diphasic and inverted T waves were present in the electrocardiogram in the nine cases in which the T sÊ loops of the vectorcardiogram were discordant or at a marked angular deviation from the QRS sÊ loop. In only two cases were the T waves normal. In these the vectorcardiogram showed a concordant T sÊ loop in all planes in one case, and a concordant T sÊ loop in two of three planes in the other case.

GROUP B (TWENTY-TWO CASES)

The Delta Wave: The characteristic delta wave, which replaced the normal septal vector, was present in every vectorcardiogram. It was oriented initially to the left in all twenty-two cases. It was additionally superiorly oriented in fourteen cases, inferiorly oriented in seven, and horizontal in one (Fig. 3).

QRS sÊ Loop—Horizontal Plane: The orientation of the QRS sÊ loop in the horizontal plane was between −60 degrees and 0 degrees in eighteen cases, and between 0 degrees and +30 degrees in four. The direction of inscription of the loop was counterclockwise in twelve cases, figure of eight in eight, and clockwise in two (Fig. 3A).

QRS sÊ Loop—Sagittal Plane: In this plane the orientation of the QRS sÊ loop was superior in fourteen cases, inferior in five and superior and inferior in three. The direction of inscription of the loop was figure of eight in nine cases, clockwise in six, double figure of eight in four, counterclockwise in two and hairpin in one.

QRS sÊ Loop—Frontal Plane: The orientation of the QRS sÊ loop in the frontal plane was

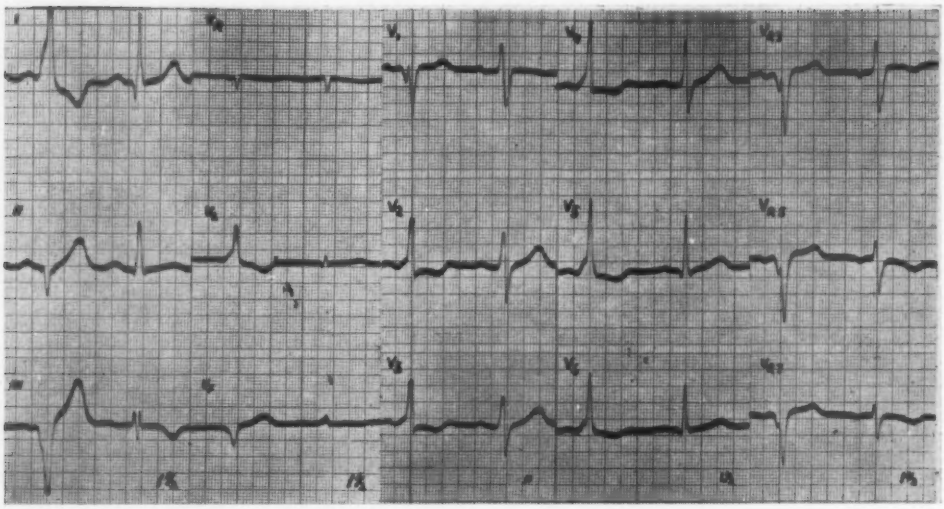

FIG. 3B. Conventional electrocardiogram showing alternate WPW and normal conduction.

to the left in all cases. The orientation superiorly and inferiorly was similar to that found in the sagittal plane. The direction of inscription of the loop was counterclockwise in sixteen, figure of eight in four and clockwise in two cases.

The T sÊ Loop: The T sÊ loop was discordant to the orientation of the QRS sÊ loop in all planes in eleven cases. It was discordant or at a marked angular deviation from the QRS sÊ loop in another seven cases. In three instances the T sÊ loop was concordant or at angular deviation or discordant to the QRS sÊ loop in one of each of the three planes. It was concordant in all planes in only one case.

Group B Electrocardiogram: The P-R interval ranged from 0.07 to 0.09 second. The QRS duration ranged from 0.10 to 0.16 second. The delta wave again was present in every case. The S-T segment was elevated 1 mm. or more in one of the extremity leads in eight cases, and in one or more of the right precordial leads in six. In twenty-one cases there were S-T segment depressions of 1 mm. or more in the extremity leads, and in seventeen there were S-T segment depressions of 1 mm. or more in one or more of the left precordial leads.

Wide or deep Q waves or QS complexes in the electrocardiogram were present in twenty cases. In fourteen, there were Q waves or QS complexes in leads III and/or aVF (Fig. 3B). A QS complex was present in leads V_1 and V_2 in ten cases.

The T wave was diphasic or inverted in two or more of the extremity leads and two or more of the precordial leads in twenty-one cases. Only in one was the T wave upright in all leads. There was left axis deviation of the electrocardiogram in sixteen and a normal axis in six.

Correlation of the Electrocardiogram and Vectorcardiogram: In this group there was also the expected correlation between the electrocardiogram and vectorcardiogram (Fig. 3). There were QS complexes or small R, deep S(rS) waves in the right precordial leads with tall R waves in the left precordial leads which correlated with the initial leftward and posterior orientation of the delta wave and QRS sÊ loop in the horizontal plane, and absence of a septal vector. Q waves or QS complexes were present in leads III and/or aVF in the fourteen cases in which the delta wave of the QRS sÊ loop was directed initially superiorly. Diphasic or inverted T waves were seen in twenty-one electrocardiograms and this correlated with the T sÊ loops that were discordant or at an abnormal angular deviation from the QRS sÊ loop. The one case in which the T waves of the electrocardiogram were normal was the case in which the T sÊ loop of the vectorcardiogram was concordant in all planes.

All of the patients with heart disease in this series fell into group B. However, since the number of patients with heart disease is relatively small, no significance can be attached to this observation. In only three patients were there normal T waves in the electrocardiogram. The remainder had abnormal T waves and no correlation could be made between the direction

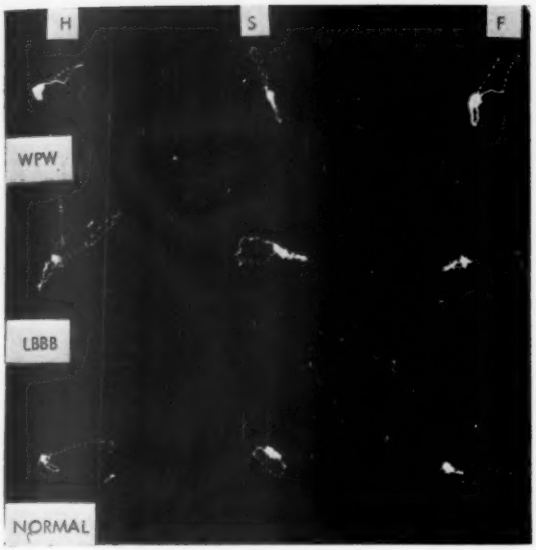

FIG. 4A. Vectorcardiograms showing WPW, left bundle branch block, and normal conduction at different times in the same patient.

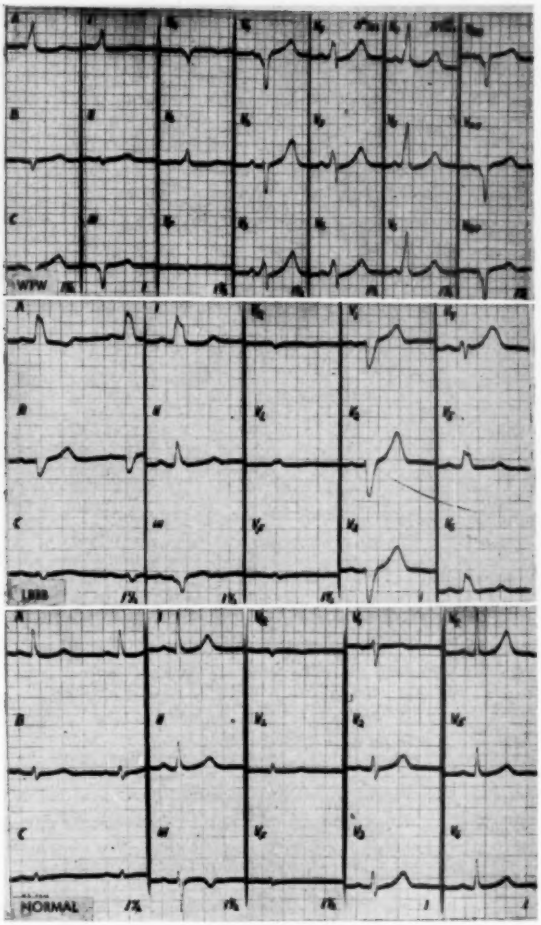

FIG. 4B. Corresponding electrocardiograms of same patient. *Top*, WPW conduction. *Center*, left bundle branch block conduction. *Bottom*, normal conduction.

of the T wave and pre-existing heart disease. It did not appear that the existence of heart disease could be diagnosed by the electrocardiogram or vectorcardiogram if the WPW syndrome was present.

The orientation of the delta wave and delta plus QRS sÊ loop in the three planes was plotted (Fig. 1). In addition, the angle between the mean direction of the delta wave and the delta plus QRS sÊ loop in each plane was calculated. In general, there was always a narrow angle between the delta wave and delta plus QRS sÊ loop, being less than 40 degrees in thirty cases in all three planes. The direction of the delta wave therefore determined the direction of the remaining portion of the QRS sÊ loop. There was no correlation between the angle formed by the delta and the delta plus QRS sÊ loop and the existence of heart disease.

MISCELLANEOUS GROUP (FIVE CASES)

Because of the presence of some atypical features that may influence the spatial orientation of the delta wave or QRS sÊ loop, five cases are grouped separately. One of them showed the criteria of group A and four those of group B.

In two patients the P-R interval of the electrocardiogram was greater than 0.12 second, measuring 0.15 second in one and 0.16 second in the other. In the latter case the patient had rheumatic heart disease with mitral and aortic valvular involvement and an enlarged left atrium. It is conceivable that delayed conduction due to atrial enlargement was responsible for the relatively long P-R interval. Although Wolff and White[25] state that the P-R interval may be normal in this syndrome, in such instances the electrocardiogram must be differentiated from that of intraventricular conduction defect, bundle branch block or ventricular hypertrophy. In the two cases of this type in our series the vectorcardiogram was helpful and showed the pathognomonic delta wave of the QRS sÊ loop.

A third patient showed three types of conduction (Fig. 4). At different times normal, left bundle branch and Wolff-Parkinson-White conduction were recorded. This occurred in a sixty-seven year old woman with vague chest

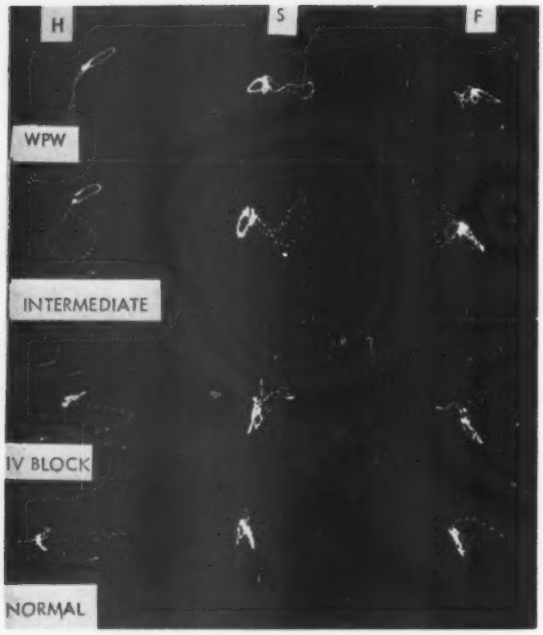

FIG. 5A. Effect of intravenous quinidine administration on WPW syndrome. Vectorcardiograms showing from top to bottom: Control (WPW), intermediate pattern, intraventricular block and normal records all obtained within ten minutes after the injection.

pain, but without palpitations or evidence of heart disease. The vectorcardiogram and electrocardiogram showed a typical Wolff-Parkinson-White syndrome, type B, superiorly oriented so that there were QS complexes in leads III and aVF (Fig. 4B). A diagnosis of diaphragmatic myocardial infarction was erroneously made. The electrocardiogram and vectorcardiogram later showed left bundle branch block and subsequently became normal, at which time no evidence of myocardial infarction could be found.

A fourth patient was a thirty-three year old man with rheumatic heart disease who was subject to paroxysms of atrial fibrillation and flutter. Electrocardiograms taken when the patient was twelve years old were normal. After the development of rheumatic heart disease with aortic stenosis, aortic insufficiency and mitral insufficiency, WPW conduction was noted. Following an attack of atrial flutter-fibrillation that lasted twenty days and terminated only after treatment with large doses of quinidine, procaine amide and digitalis, normal conduction was restored and the vectorcardiogram and electrocardiogram showed left ventricular hypertrophy. In this instance the WPW conduction masked the pattern of left ventricular hypertrophy.

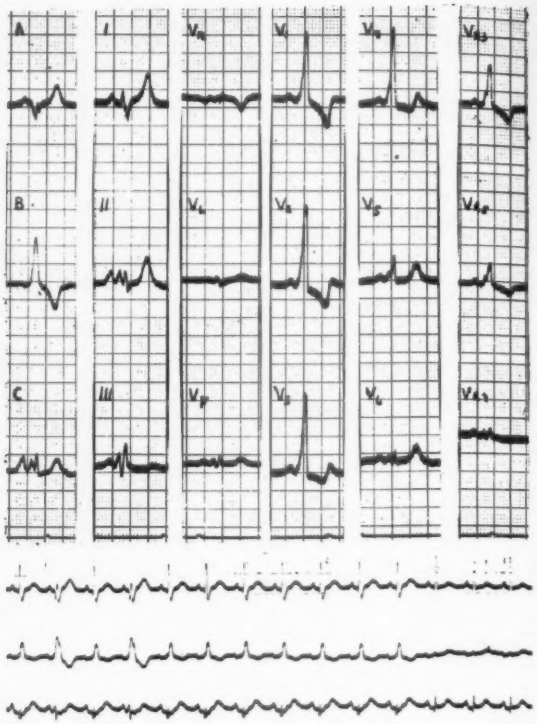

FIG. 5B. *Top*, control electrocardiogram of same patient showing WPW conduction. *Bottom*, component leads A, B and C following intravenous administration of quinidine. The second and fourth complexes correspond to the intermediate pattern of the vectorcardiogram. The last three complexes are normal, and the remaining complexes correspond to the intraventricular block pattern of the vectorcardiogram.

In the fifth patient an effort to obtain further information on the course of the spread of excitation in the WPW syndrome was made by administration of intravenous quinidine. Continuous vectorcardiograms and simultaneous three-lead electrocardiograms were taken for the ensuing twenty minutes (Fig. 5). The control vectorcardiogram taken before quinidine was administered (Fig. 5A) shows a typical WPW pattern directed anteriorly (type A). Two minutes and fifteen seconds after the administration of quinidine the QRS sÊ loop in the horizontal plane enlarged and widened, but the orientation remained the same. Conduction delay was noted not only in the initial portion of the QRS sÊ loop, but also during the first half of the loop. The corresponding electrocardiogram (Fig. 5B) showed a short P-R interval but the QRS was wider than the control. This complex due to the effect of quinidine was considered to be an intermediate tracing between WPW and the subsequent patterns.

After two minutes and forty-five seconds had elapsed, only intraventricular block was noted. This was characterized on the vectorcardiogram by the disappearance of the delta wave. The QRS sÊ loop was directed anteriorly and superiorly whereas previously it was anterior and horizontal. The direction of inscription of the QRS sÊ loop in the horizontal plane was clockwise whereas it had previously been inscribed in a figure of eight fashion. No delta wave was present, and there was conduction delay in the terminal portion of the QRS sÊ loop. After ten minutes had elapsed the vectorcardiogram and electrocardiogram became normal.

In many of the cases the electrocardiogram exhibited the so-called "concertina effect," described by Ohnell,[26] consisting of a progressive lengthening of the P-R interval and narrowing of the QRS complex which assumes a more normal configuration (Fig. 6). This phenomenon has been attributed to varying degrees of anomalous conduction in the same patient changing progressively from complex to complex.

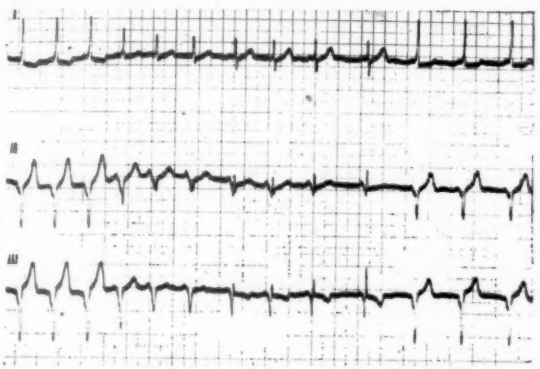

FIG. 6. "Concertina effect." After the first three or four cycles which show WPW conduction, note the gradual appearance of normal QRS complexes and lengthening of the P-R interval and then a return to anomalous conduction.

COMMENTS

In our study the mean delta vector was anteriorly directed and parallel to the sagittal plane in approximately one-third of the cases. By definition these cases were classified into group A (Fig. 1). In two-thirds of the cases, the mean delta vector was oriented to the left in the horizontal plane and by definition were classified into group B. Electrocardiographically these two groups correspond to types A and B of Rosenbaum et al.[9] Their classification was based upon the configuration of the QRS in V_1, not solely on the delta portion of the QRS, but there was very little difference between the spatial angle of the mean delta vector and the entire delta plus QRS sÊ vector in the horizontal plane (Fig. 1).

In seven cases we were able to obtain vectorcardiograms during WPW and normal conduction (Figs. 2 and 3). We were impressed with the difference in the appearance of the QRS sÊ loops. The orientation of the QRS sÊ loops during WPW conduction in all planes appears so different from the normal, that it is hard to conceive that the dissimilarity is due to the addition of a delta vector to the normal vector. Not only the initial but also the terminal portion of the QRS sÊ loop is changed during WPW conduction. We therefore conclude that the entire course of the spread of the wave of excitation to both ventricles may be altered.

Arrhythmias: The common occurrence of tachycardia in this syndrome is of great interest and importance, and although in most instances the arrhythmia is considered to be benign, there have been reported cases of sudden death occurring as a consequence of the tachycardia.[27]

In the majority of cases a tachycardia of the supraventricular type is responsible for the rapid heart action[28] (Fig. 7). Usually, normal A-V conduction replaces the anomalous conduction when tachycardia of this type occurs, and at that time it is impossible to make a diagnosis of the WPW syndrome unless one has a previous cardiogram showing the typical features. Figure 7 shows the rare occurrence of right bundle branch block during an episode of spontaneous tachycardia.

Less frequently, atrial flutter or fibrillation occurs, and in such instances anomalous conduction usually persists, and may be an important clue to the mechanism of conduction.[23] Figure 8 is an example. Often an erroneous diagnosis of a ventricular tachycardia is made, and according to Wolff[23] and also Langendorf[27] most examples of ventricular tachycardia reported in this syndrome when subjected to rigid interpretation were not bona fide cases but usually atrial flutter or fibrillation with anomalous conduction.

Treatment of Tachycardias: When paroxysms of tachycardia become frequent, prolonged or disturbing to the patient, the conduction should be normalized. If myocardial infarction is suspected one must normalize conduction

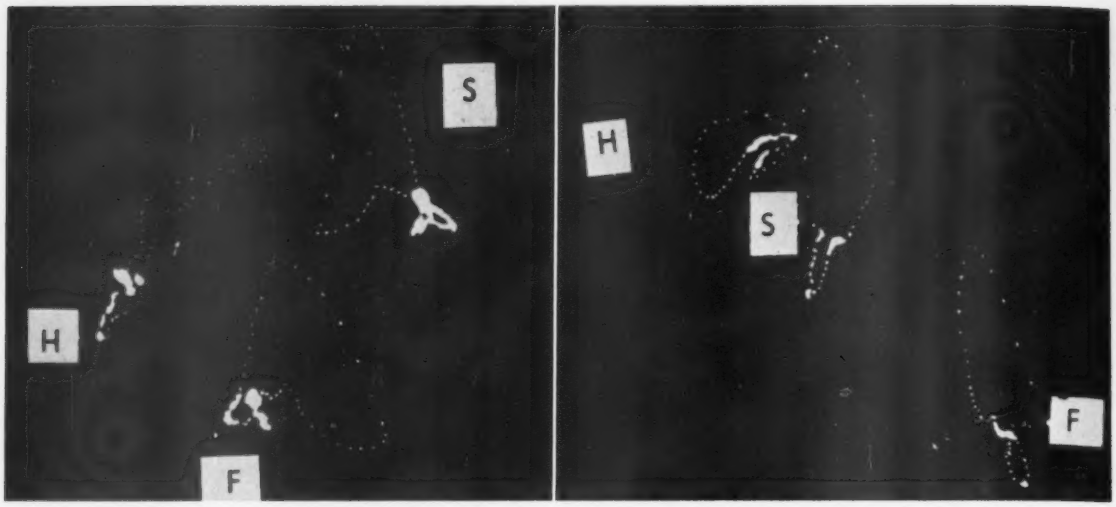

FIG. 7A. Vectorcardiograms showing WPW conduction (*left*) and right bundle branch block (*right*) during an attack of paroxysmal tachycardia.

in order to obtain an accurate diagnosis.[29,30]

A variety of maneuvers and drugs has been effective in temporarily abolishing anomalous conduction. Digitalis favors the anomalous conduction[23,28,31] and for that reason is usually ineffective in the treatment of atrial flutter or fibrillation.[23,28] When atrial flutter or fibrillation persists, or when paroxysms of supraventricular tachycardia become frequent or prolonged, quinidine is the drug of choice.[28] Procaine amide is also effective. Rarely quinidine and digitalis must be used concomitantly to abolish an attack of flutter or fibrillation. In the patient previously described, who had an episode of atrial flutter-fibrillation that lasted twenty days, the administration of quinidine, procaine amide and digitalis was necessary to abolish the arrhythmia.

Atropine, amyl nitrite and phenylephrine are occasionally effective in restoring normal conduction [29,30,32] but use of these drugs for permanent conversion is impractical because their action is usually transient.

Hemodynamic Studies: Ferrer and associates[13] studied two patients with the WPW syndrome. Right heart catheterization was employed to determine pressures and cardiac output. During paroxysmal A-V nodal tachycardia there were marked pressure and presumably filling abnormalities in the right atrium that were related to tricuspid insufficiency, yet the cardiac output was unchanged. During normal sinus rhythm and anomalous conduction, intracardiac pressures, arterial blood pressure and systemic blood flow were normal in one of the two cases. Electrokymographic studies by Samet et al.[14]

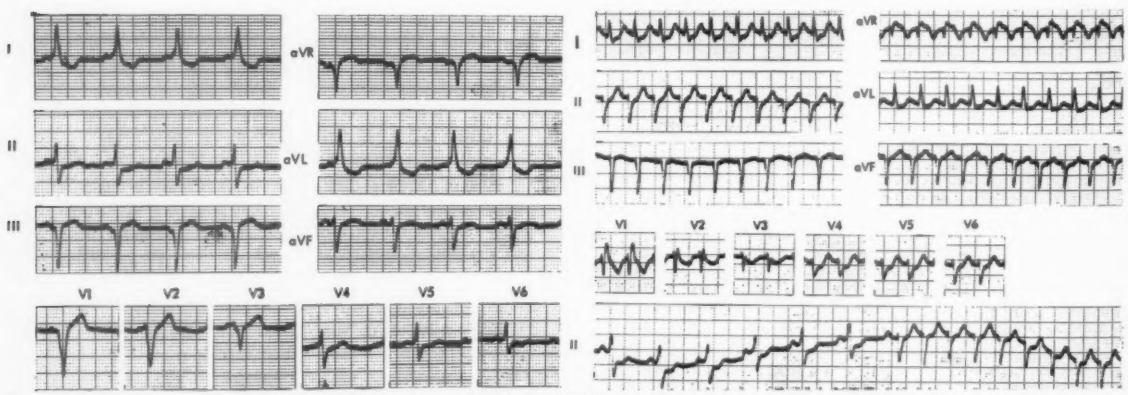

FIG. 7B. Electrocardiograms of same patient showing WPW during normal sinus rhythm (*left*) and right bundle branch block during paroxysmal tachycardia (*right*). Note continuous record of lead II showing the abrupt onset of a paroxysm of tachycardia.

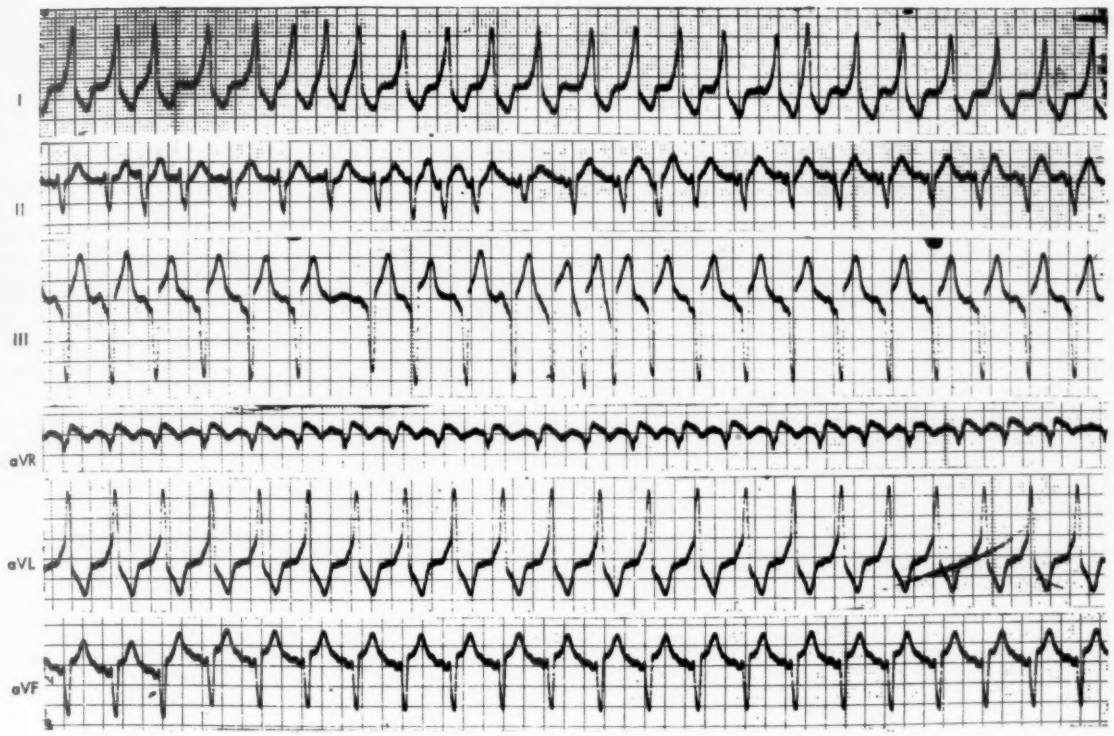

FIG. 8. Atrial flutter-fibrillation with anomalous (WPW) conduction. In lead aVR a regular 2:1 flutter is seen. In leads I, II and III the rhythm is irregular (fibrillation). Aberrant ventricular conduction (WPW) persists and the delta wave is clearly seen in leads I and aVL.

and Dack et al.[15] showed that in the majority of cases of this syndrome there was no abnormal asynchronism of ventricular contraction.

Myocardial Infarction; Pitfalls in Diagnosis in the Presence of WPW Conduction: The diagnosis of myocardial infarction is doubly difficult. In acute myocardial infarction and normal conduction there is loss of the initial septal vector or the beginning of the QRS sÊ loop, which is indicated electrocardiographically by a Q wave. However, in the presence of Wolff-Parkinson-White syndrome, the delta wave replaces the initial forces of the QRS. If myocardial infarction has occurred, in the leads in which the delta wave is upright diagnostic Q waves are not observed. In addition, because the QRS sÊ loop is so often oriented superiorly (Figs. 3 and 4) there are frequently QS complexes in leads III and aVF of the electrocardiogram, and a diagnosis of diaphragmatic myocardial infarction may be erroneously made. The S-T segment and T wave abnormalities that are so commonly present in this syndrome are of no diagnostic value and should not be misinterpreted as being additional evidence of myocardial infarction. These facts were clearly brought out by Wolff and Richman[29] and Grayzel.[30]

SUMMARY

1. Thirty-eight cases of Wolff-Parkinson-White syndrome are analyzed by vectorcardiographic and electrocardiographic correlative study.

2. Although electrocardiographic grouping into types A and B has been challenged as being unnecessary, vectorially the delta vector or QRS sÊ loops in the horizontal plane fell into two distinct quadrants which we have designated as groups A and B, respectively. In group A the delta vector is anteriorly oriented, and in the +30 degrees and +120 degrees quadrant in the horizontal plane. In group B the delta vector is oriented to the left, and in the −60 degrees to +30 degrees quadrant in the horizontal plane. In group A the QRS sÊ loop was more commonly inferiorly oriented, whereas in group B the QRS sÊ loop was more commonly superiorly oriented, although there was overlap.

3. The delta portion of the QRS sÊ loop was usually oriented in the same direction as the remainder of the QRS sÊ loop, and determined the spatial orientation of the QRS sÊ loop.

4. Some of the clinical features of this syndrome are briefly discussed, including the association with paroxysmal tachycardia and atrial fibrillation or flutter.

5. The pitfalls in the diagnosis of myocardial infarction in the presence of this syndrome are stressed.

6. In patients whose conduction became normal the QRS sÊ loops that were observed were usually greatly dissimilar from those recorded during WPW conduction. This observation, in conjunction with the electrokymographic and catheterization studies of others which demonstrated no abnormal asynchronysm of ventricular contraction, suggests to us that early excitation of just one ventricle cannot take place, and that therefore not only the initial portion of spread of excitation is anomalous, but also the entire conduction through both ventricles may be anomalous.

Acknowledgments

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References

1. Wilson, F. N. A case in which the vagus influenced the form of two ventricular complexes of the electrocardiogram. *Arch. Int. Med.*, 16: 1008, 1915.
2. Wedd, A. M. Paroxysmal tachycardia with reference to normotropic tachycardia and the role of the extrinsic cardiac nerves. *Arch. Int. Med.*, 27: 571, 1921.
3. Wolff, L., Parkinson, J. and White, P. D. Bundle branch block with short PR interval in healthy young people prone to paroxysmal tachycardia. *Am. Heart J.*, 5: 685, 1930.
4. Holzmann, M. and Scherf, D. Uber Elektrokardiogramme mit verkuerzter Vorhof-Kammer-Distanz und positiven P-Zacken. *Ztschr. klin. Med.*, 121: 404, 1932.
5. Wolferth, C. C. and Wood, F. C. The mechanism of production of short P-R intervals and prolonged QRS complexes in patients with presumably undamaged hearts: Hypothesis of an accessory pathway of auriculoventricular conduction (bundle of Kent). *Am. Heart J.*, 8: 297, 1933.
6. Butterworth, J. S. and Poindexter, C. A. Fusion beats and their relation to the syndrome of short PR interval associated with a prolonged QRS complex. *Am. Heart J.*, 28: 149, 1944.
7. Segers, M., Lequime, J. and Denolin, H. L'activation ventriculaire precoce de certains coeurs hyperexcitables. Etude de l'onde de l'ectrocardiogramme. *Cardiologia*, 8: 113, 1944.
8. Hunter, A., Papp, C. and Parkinson, J. The syndrome of short PR interval, apparent bundle branch block, and associated paroxysmal tachycardia. *Brit. Heart J.*, 2: 107, 1940.
9. Rosenbaum, F. F., Hecht, H. H., Wilson, F. N. and Johnston, F. D. The potential variations of the thorax and the esophagus in anomalous atrioventricular excitation (Wolff-Parkinson-White syndrome). *Am. Heart J.*, 29: 281, 1945.
10a. Sodi-Pallares, D., Soberon, J., Thomsen, P., Fishleder, B. L. and Estandia, A. Contribucional estudio del sindrome de W.P.W. por las derivaciones intracavitarias. *Arch. Inst. cardiol. Mexico*, 8: 1, 1948.
10b. Sodi-Pallares, D. and Calder, R. New Concepts in Electrocardiography. St. Louis, 1956. C. V. Mosby Co.
11. Grishman, A., Kroop, I. G. and Steinberg, M. F. The course of the excitation wave in patients with electrocardiograms showing short PR intervals and wide QRS complexes (Wolff-Parkinson-White syndrome). *Am. Heart J.*, 40: 554, 1950.
12. Prinzmetal, M., Kennamer, R., Corday, E., Osborne, J. A., Fields, J. and Smith, L. A. Accelerated Conduction. New York, 1952. Grune & Stratton.
13. Ferrer, M. J., Harvey, R. M., Weiner, H. M., Cathcart, R. T. and Cournand, A. Hemodynamic studies in two cases of Wolff-Parkinson-White syndrome with paroxysmal A-V nodal tachycardia. *Am. J. Med.*, 7: 725, 1949.
14. Samet, P., Mednick, H. and Schwedel, J. B. Electrokymographic studies in the relation between the electrical and mechanical events of the cardiac cycle in Wolff-Parkinson-White syndrome. *Am. Heart J.*, 40: 430, 1950.
15. Dack, S., Paley, D. H. and Brahms, S. S. The electrokymogram in Wolff-Parkinson-White syndrome. *Am. Heart J.*, 41: 437, 1951.
16. Grant, R. P., Tomlinson, F. B. and Van Buren, J. K. Ventricular activation in the pre-excitation syndrome (Wolff-Parkinson-White). *Circulation*, 18: 355, 1958.
17. Duchosal, P. W. and Sulzer, R. La Vectocardiographie. Basle, 1949. S. Karger.
18. Donzelot, E., Milovanovich, J. B. and Plavsic, C. Vectographic spatiale frontale et horizontale due syndrome de Wolff, Parkinson, et White. *Arch. mal. coeur*, 8: 781, 1949.
19. Grishman, A. and Jaffe, H. L. Spatial vectorcardiography: wide QRS complexes with short PR interval (the Wolff-Parkinson-White syndrome). *J. Mt. Sinai Hosp.*, 18: 208, 1951.
20. Cernohorsky, J. A vector analysis of the W.P.W. syndrome. *Cardiologia*, 29: 278, 1956.
21. Friedberg, C. K. Diseases of the Heart, 2nd ed. Philadelphia, 1956. Saunders.
22. Odler, J., Montouchet, M. and Duchosal, P. W. Etude spatiale de la compasante prematuree dans le syndrome de Wolff-Parkinson-White. *Cardiologia*, 30: 182, 1957.
23. Wolff, L. Syndrome of short P-R interval with abnormal QRS complexes and paroxysmal tachycardia (Wolff-Parkinson-White syndrome). *Circulation*, 10: 282, 1954.
24. Grishman, A., Borun, R. and Jaffe, H. L. Spatial vectorcardiography: Technique for the simulta-

neous recording of the frontal, sagittal and horizontal projections. I. *Am. Heart J.*, 41: 483, 1951.

25. Wolff, L. and White, P. D. Syndrome of short P-R interval and abnormal QRS complexes and paroxysmal tachycardia. *Arch. Int. Med.*, 82: 446, 1948.
26. Ohnell, R. F. Pre-excitation, a cardiac abnormality. *Acta med. scandinav.* (Suppl.) p. 152, 1944.
27. Langendorf, R., Lev, H. and Pick, R. Auricular fibrillation with anomalous A-V excitation imitating ventricular paroxysmal tachycardia. A case report with clinical and autopsy findings and a critical review of the literature. *Acta cardiol.*, 7: 241, 1952.
28. Katz, L. and Pick, R. Clinical Electrocardiography; The Arrhythmias. Philadelphia, 1956. Lea and Febiger.
29. Wolff, L. and Richman, J. L. The diagnosis of myocardial infarction in patients with anomalous atrio-ventricular excitation (Wolff-Parkinson-White syndrome). *Am. Heart J.*, 45: 545, 1953.
30. Grayzel, J. The electrocardiographic criteria in the differential diagnosis of the pre-excitation (Wolff-Parkinson-White) syndrome and arteriosclerotic heart disease. *New England J. Med.*, 259: 369, 1958.
31. Fox, T. T., Travell, J. and Molorsky, L. Action of digitalis on conduction in the syndrome of short P-R interval and prolonged QRS complex. *Arch. Int. Med.*, 71: 206, 1943.
32. Blinder, H., Burnstein, J. and Smelin, R. Drug effects in Wolff-Parkinson-White syndrome. *Am. Heart J.*, 44: 268, 1952.

Vectorial Interpretation of the Ventricular Complex in Wolff-Parkinson-White Syndrome*

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THE ELECTROCARDIOGRAPHIC syndrome (WPW) described by Wolff, Parkinson and White in 1930 is characterized by a short P-R interval and a widened QRS complex, with a slurred initial portion considered as the "delta wave." The frequent association of this anomaly with crises of paroxysmal tachycardia, its occurrence with certain types of congenital heart disease, the possibility of confusion with the patterns of myocardial infarction of the diaphragmatic region, and its prognosis, have already been the subjects of many papers.[1–5]

The electrogenesis of this anomaly has been a matter of frequent controversy. An example of this is found in the extensive review of the literature made in 1944 by Ohnell.[6] He found forty hypotheses for the electrogenesis of the syndrome. Others[7] were added at a later date.

A recent symposium[8] regarding this anomalous A-V activation showed unanimous opinion among researchers that the ventricular complexes of the WPW syndrome depend on a double ventricular activation. According to Schafer's theory,[9] the first activation is due to the premature excitation of approximately 9 per cent of the total ventricular muscle. The second is due to the activation of the ventricles by the natural physiologic pathway. As a result of this, we have a complex that is comparable to a fusion beat. However, we disagree about the mechanism of preactivation.

Sodi-Pallares and collaborators[10] state that the delta wave represents the premature activation of a zone in the septal mass which has a lower than normal threshold of excitability, brought about by electronic waves emanated during atrial depolarization. On the other hand, Prinzmetal[8] observed experimentally that the excitation of each portion of the A-V node corresponds to a particular morphology of the QRS, and he correlated the appearance of the WPW syndrome with activation of definitive zones of the node. He concluded that (1) the A-V node has a structure similar to the central nervous system, having certain regions that are responsible for the activation of specific portions of the ventricular musculature; and (2) the morphology of the WPW syndrome results from a special conduction disturbance in one of these portions of the A-V node, where the delay of the stimulus is shortened, causing an accelerated conduction.

This and other accumulated data (e.g., the appearance of this anomaly during anesthetic induction and intracardiac catheterization, and the impossibility of coexistence of WPW conduction with complete A-V block) make the hypothesis of the stimulus conduction by anomalous anatomic pathways[8] much less probable.

Because there are many different viewpoints on the electrogenesis of the syndrome, we thought it would be of interest to determine: (1) whether or not a relationship exists between the spatial orientation of the vector that represents the "pre-excitation wave" and the zones of the ventricular mass where complexes similar to the syndrome were experimentally obtained; and (2) what value such spatial analysis would have in clinical electrocardiography.

Several authors[11,12] have studied the vectorcardiographic loop in the WPW syndrome. However, in reviewing the literature, we found

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TABLE I

Clinical Data and Vectoral Analysis of Twenty-Two Cases of WPW Syndrome, Type I

Case No.	Age (yr.) and Sex	SÂΔ (in degrees)			SÂQRS (in degrees)			SÂT (in degrees)			SÂΔ-SÂQRS (degrees)	Clinical Diagnosis
		F	H	S	F	H	S	F	H	S		
1	40, F	− 45	+ 40	−140	− 15	+ 5	−100	+ 90	+ 90	+125	26	Normal
2	40, M	− 30	+ 10	−110	− 35	+ 25	−125	+ 75	− 20	+ 80	29	Normal
3	30, M	− 30	+ 10	−100	− 45	− 10	− 80	+110	+125	+100	25	Normal
4	63, M	− 20	+ 15	−130	− 30	+ 30	−140	+120	−160	+ 75	18	ASHD*
5	36, F	− 20	+ 30	−160	− 5	− 5	− 70	+110	+100	+160	35	HHD†
6	29, M	− 20	+ 45	−150	− 40	+ 45	−140	+ 80	− 75	+ 45	20	CCP‡
7	56, F	− 15	+ 20	−140	− 20	+ 15	−115	− 20	+ 60	−160	15	Normal
8	56, M	− 15	+ 20	−140	− 20	+ 10	−110	+140	+175	+ 95	17	ASHD
9	28, M	− 10	+ 60	−170	− 45	+ 75	−160	+ 80	+ 30	+100	15	Normal
10	16, F	− 5	+ 55	+175	− 20	+ 20	−130	+ 85	+ 60	+100	28	RHD§
11	20, M	+ 10	+ 20	+140	+ 20	− 20	+ 50	+ 40	+ 50	+135	40	RHD
12	24, F	+ 25	+ 25	+140	+ 20	+ 15	+120	+135	−160	+ 75	13	RHD
13	35, F	+ 30	+ 10	+100	+ 70	− 60	+ 60	+ 25	+ 45	+160	60	Chagas
14	50, F	+ 35	+ 25	+125	0	− 65	0	+170	+135	+150	90	ASHD
15	46, M	+ 60	+ 60	+125	− 20	+ 50	−160	+ 85	− 80	+ 50	75	Normal
16	19, F	+ 65	+ 30	+110	+ 60	− 15	+ 80	−120	+165	−100	35	RHD
17	26, F	+ 80	+ 25	+100	+ 20	+ 30	+135	+ 70	− 70	+ 50	50	Normal
18	18, M	+ 90	+ 90	+105	+ 75	+ 15	+ 95	− 80	+ 15	− 95	33	RHD
19	29, M	+100	+110	+120	+100	+120	+115	+ 65	− 5	+ 80	10	Normal
20	35, F	+110	+160	+115	+ 75	+ 20	+ 85	+ 60	+ 25	+100	45	Normal
21	35, M	+120	+115	+165	+ 95	+ 95	+130	− 90	− 90	− 40	40	Chagas
22	30, M	+120	+150	+110	+ 90	+ 90	+140	+ 50	+ 15	+135	45	Normal

* ASHD = arteriosclerotic heart disease.
† HHD = hypertensive heart disease.
‡ CCP = chronic cor pulmonale.
§ RHD = rheumatic heart disease.

TABLE II

Clinical Data and Vectorial Analysis of Five Cases of WPW Syndrome, Type II

Case No.	Age (yr.) and Sex	SÂΔ (in degrees)			SÂQRS (in degrees)			SÂT (in degrees)			SÂΔ-SÂQRS (degrees)	Clinical Diagnosis
		F	H	S	F	H	S	F	H	S		
1	24, F	−30	−15	−60	−40	0	−90	+130	+150	+120	23	HHD*
2	24, F	−20	− 5	−75	−35	−10	−80	+110	+100	+160	15	Normal
3	42, M	0	−10	0	0	−30	0	+175	+130	+170	16	Chagas
4	8, M	+ 5	−20	0	−30	−70	−10	+125	+130	+120	43	Chronic nephritis
5	43, M	+45	−10	+80	+15	−30	+30	−120	+120	−165	40	ASHD†

* HHD = hypertensive heart disease.
† ASHD = arteriosclerotic heart disease.

that Genohorsky[13] was the only author to analyze the delta wave of the electrocardiogram vectorially, and his conclusions do not totally agree with ours.

Material and Methods

Material: Among 31,822 electrocardiographic tracings, of which 26,034 were taken from the files of the Electrocardiographic Department of the Hospital das Clinicas of the University of Sao Paulo and 5,788 from our private practice, we found twenty-seven cases (0.085 per cent) showing the WPW syndrome. Fifteen of these tracings were of males and twelve of females. The ages varied from eight to sixty-three years (average 33.4 years). Tables I and II show the clinical diagnosis of our cases.

Methods: An analysis of the vectors representing the "pre-excitation" wave (SÂΔ) and the total ventricular activation (SÂQRS) was made, taking into

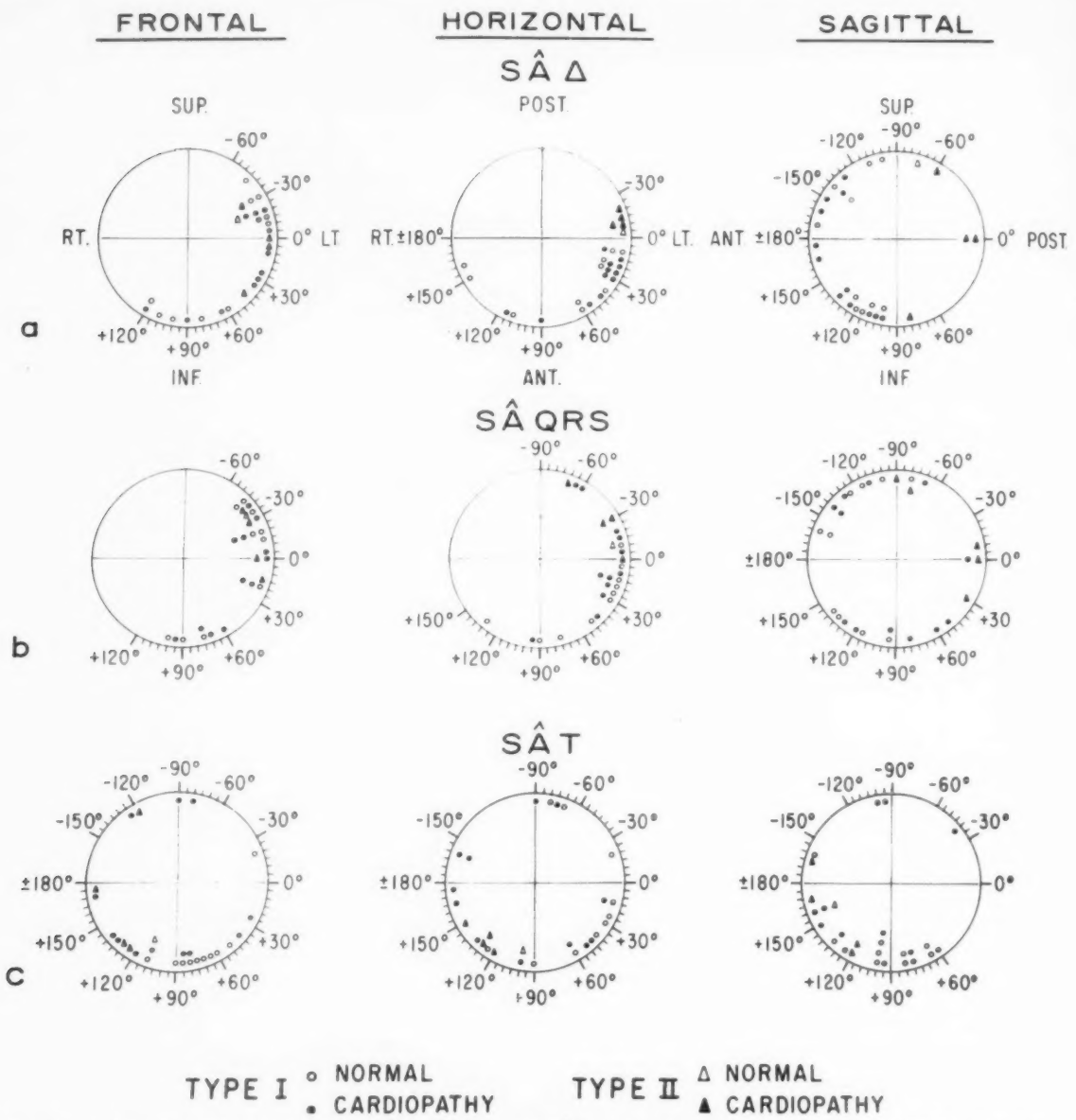

FIG. 1. a, b and c, Orientation of the SÂΔ, SÂQRS and SÂT vectors in twenty-seven cases of WPW syndrome.

consideration the area of the deflections in each lead of the frontal plane and of the horizontal plane (leads V_1 to V_6). The "electrical center" of the heart was considered as projecting anteriorly at the level of lead V_2 and we utilized the model described by Peñaloza and Tranchesi[14] for spatial determination of the vectors.

Using only the orientation of the "pre-excitation" or delta wave vector in the horizontal plane, independent of the morphology of the QRS complex in the precordial leads, the tracings were divided, for practical purposes, into two types: *type I*, when the initial delta wave was positive in lead V_2 (SÂ vector oriented forward), and *type II*, when the premature excitation wave was negative in lead V_2 (SÂ vector directed backward).

RESULTS

The results of the analytical study of the SÂΔ, of the vectors that represent the ventricular electrical events and of the SÂΔ-SÂQRS spatial angle are shown in Tables I and II.

The spatial position of these vectors will be discussed individually for each variable.

I. The SÂΔ Vectors: These are distributed as follows (Fig. 1a): (A) *Frontal Plane:* In type I

its orientation varied from −45 degrees to +120 degrees (average +45.7 degrees), but in type II it varied from −30 degrees to +45 degrees (average zero degrees). (B) *Horizontal Plane:* In type I, as in the initial classification, the vector of the pre-excitation wave always pointed forward from +10 degrees to +160 degrees (average +51.1 degrees); in type II by contrast, it pointed backward with slight variation from −5 degrees to −20 degrees (average −12 degrees). (C) *Sagittal Plane:* The orientation of the delta wave vector varied from +100 degrees to −100 degrees (average +165 degrees), pointing forward in type I and from +80 degrees to −75 degrees in type II.

II. The SÂQRS Vectors: The positions of these vectors were as follows (Fig. 1b): (A) *Frontal Plane:* The distribution of ÂQRS ranged from −45 degrees to +100 degrees (average +15 degrees) in type I and from −40 degrees to +15 degrees (average −18 degrees) in type II. (B) *Horizontal Plane:* In this plane there was a great dispersion in the localization of the ventricular activation vector; in type I it was oriented from −65 degrees to +130 degrees (average +22 degrees), forward in 72.7 per cent of the cases and backward in 27.3 per cent. In type II the variation was from 0 degrees to −70 degrees, all the vectors pointing backward.

(C) *Sagittal Plane:* As in the horizontal plane, the dispersion was also great since the vectors in type I occupied practically all the quadrants. In type II the axes were directed backward, varying from +30 degrees to −90 degrees.

III. The SÂT Vectors: These showed the following distributions (Fig. 1c): (A) *Frontal Plane:* In type I, the ÂT presented a great dispersion (average +123.6 degrees). However, none was registered within the limits of −20 degrees to −80 degrees. In type II, the ÂT vector was situated between +110 degrees and −120 degrees. (B) *Horizontal Plane:* In this plane the vector of the ventricular repolarization in type I was localized in all sextants, with 63.2 per cent of the cases oriented forward; in type II it varied from +100 degrees to +150 degrees (average +122 degrees), always pointing forward. (C) *Sagittal Plane:* The T vector in type I was not situated in the section between −40 degrees to −95 degrees only. On the other hand, it was oriented from −165 degrees to +120 degrees (average −153 degrees) in type II.

IV. SÂΔ—SÂQRS Angle: Finally, the values obtained from the SÂΔ—SÂQRS angle also differed for each type. The maximum value in type I was 90 degrees and the minimum was 10 degrees (average 34.7 degrees). In type II these values were 43 degrees and 15 degrees, respectively, with a mean value of 27.4 degrees.

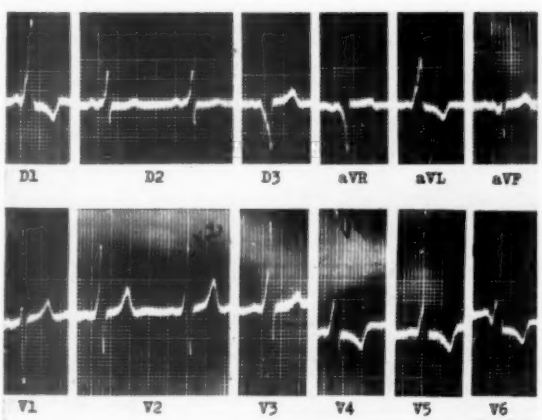

FIG. 2. Case 8. WPW syndrome, type I. Note positive delta wave in lead V_2.

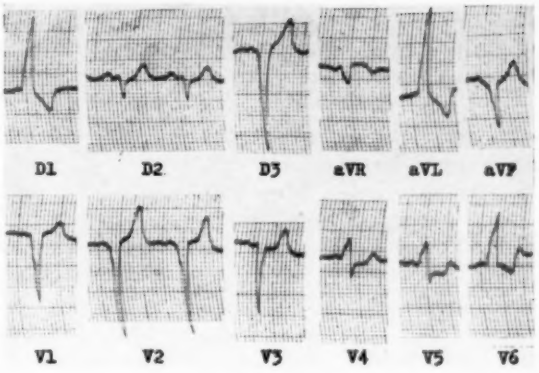

FIG. 3. Case 2. WPW syndrome, type II. Note negative delta wave in leads V_1 and V_2.

COMMENTS

Vectorial Classification of the WPW Syndrome: There are many electrocardiographic classifications of the WPW syndrome, but Rosenbaum's classification is most frequently utilized. In his classification two types are considered: type A showing a positive delta wave with an absent or small S wave in all precordial leads, and type B, with a negative delta wave and large S waves in lead V_1 or leads V_1 and V_2. However, in analyzing our material, we verified the existence of cases of the WPW syndrome with a positive delta wave in the right precordial leads (SÂΔ oriented forward) and large S waves in the same leads, which makes it difficult to classify these tracings. For these reasons we

thought that it would be of interest to classify the electrocardiograms, taking into consideration only the spatial orientation of the pre-excitation or delta wave.

Tracings that show the SÂΔ oriented forward (positive delta wave in lead V_2 or in leads V_1 and V_2) independent of the morphologies of the QRS complexes in the right precordial leads (Fig. 2), we call type I. In this group the SÂQRS can be oriented backward (27.2 per cent of the cases) with a predominance of negativities in lead V_2. Type II is characterized by the backward orientation of the SÂΔ (negative delta wave in lead V_2) (Fig. 3). We believe that this classification is simpler and applicable to almost all the cases of WPW syndrome, for it allows us to anticipate, to a certain extent, the probable localization of the delta wave focus of origin.

Relationship Between the SÂΔ and the Focus of Origin of the "Pre-Excitation" Wave: Experimentally[10] it has been possible to register morphologies similar to the WPW syndrome (type A or type B) by the excitation of determined regions of the interventricular septum and of the ventricular walls. It is very probable that the focus of origin of the "pre-excitation" wave in type I of the WPW syndrome is situated in the previously described parts of the ventricles, such as the posterobasal regions of the septum and adjacent areas of the ventricular walls, due to the spatial orientations of the SÂΔ in this type—forward, either to the left (as happened more frequently) or to the right. On the other hand, in type II with the SÂΔ oriented backward and to the left, the region of premature excitation would be localized in the anterior and right aspect of the septum and in the right ventricular anterior wall (Fig. 4).

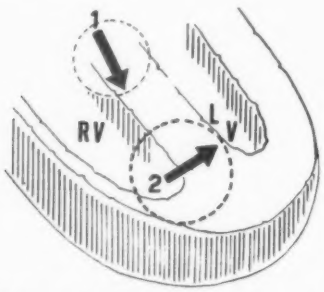

FIG. 4. Horizontal view of the heart. Approximate localization of the focus of origin of the "pre-excitation" wave in WPW syndrome, types I and II.

Analysis of the SÂΔ-SÂQRS Angle: The small spatial angle obtained between the SÂΔ and the SÂQRS vectors in the two types of the WPW

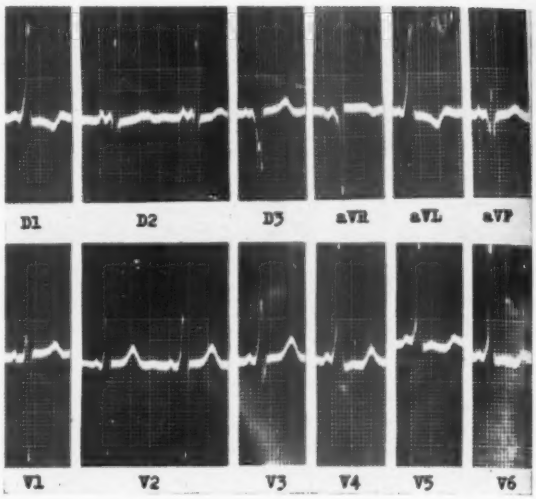

FIG. 5. Case 5. WPW syndrome, type I, with SÂQRS backwardly oriented in a patient presenting accentuated arterial hypertension. Note deeper S wave than R wave in leads V_1 and V_2 with positive delta wave.

syndrome suggests a definite influence of the electrical forces that are developed during the premature activation upon the mean orientation of the total ventricular activation. For this reason, we believe it is logical to conclude that when a tracing showing the WPW syndrome shows a great deviation between the SÂΔ and SÂQRS there exists the possibility of the presence of a pathologic factor that could be responsible for the great angle registered.

The analysis of our material did not permit a safe appreciation of this possibility even though the angles were slightly greater in the pathologic cases (Tables I and II).

Comments on the WPW Syndrome Type I, Showing Deep S Waves in the Right Precordial Leads: In Rosenbaum's original classification, he considered the WPW syndrome, type A as being a combination of the forward orientation of the delta wave and the Rs type of ventricular complex. However, as we have already described, in many cases of our material, we observed deep S waves in leads V_1 and V_2 with SÂΔ oriented forward (instances of type I).

By assuming that increased left ventricular potentials, related to overloading of this chamber, could contribute to the registration of the backwardly oriented SÂQRS with forwardly oriented SÂΔ, we correlated these findings with the presence or absence of cardiopathy. Thus five of six patients with the WPW syndrome, type I, showing S waves bigger than the R waves in leads V_1 and V_2, presented clinically and

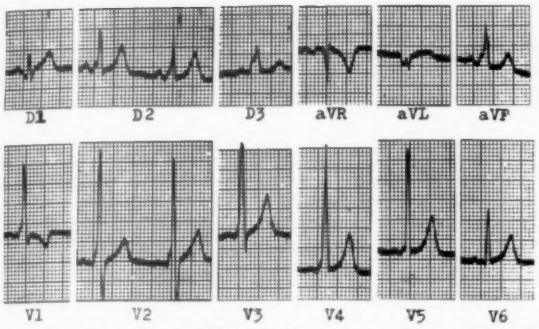

FIG 6. Case 22. WPW syndrome, type I, in a normal person. Observe the positive T waves in leads V_3, V_4, V_5 and V_6 and the Q waves in leads I and V_6. SÂΔ situated at +120° in the frontal plane (isoelectric in aVR).

radiologically clear signs of left ventricular overloading (Fig. 5) and only one was considered as having a normal left ventricle.

Relationship Between the Polarity of the T Waves (Not Opposed to Sense of the QRS Complexes) and the Heart Condition: We have noted that a great number of patients showing the WPW syndrome with positive T waves also have positive QRS complexes in leads V_4, V_5 and V_6 (Fig. 6), and that most of them did not present cardiopathies (only two of eleven patients had cardiac lesions of the mitral insufficiency type). The other eleven patients showing a negative T wave in leads V_5 and V_6 had clinical and radiologic signs of left ventricular overloading. In the remaining five patients with flat or isoelectric T waves, only three presented a large left ventricle, so that when we deal with this morphology, nothing can be inferred.

Possibility of the Existence of the WPW Syndrome Presenting Q Waves in the Left Precordial Leads: Some authors[16] have mentioned the absence of Q waves in leads V_5 and V_6 as among the morphologic characteristics of the QRS complex in cases of the WPW syndrome. However, we had the opportunity of studying a patient showing a permanent WPW syndrome, type I, in whom a definite delta wave could be registered in lead V_1 simultaneously with a Q wave in leads V_6 and V_7 (Fig. 7). Reviewing the other three cases with the pre-excitation wave situated at the right of +90 degrees in the frontal plane (negative delta wave in lead I), we found that all three presented Q waves in lead V_6 (Fig. 6).

It can be concluded, therefore, that Q waves can be present in the left precordial leads in cases of the WPW syndrome, type I, depending upon the orientation of the SÂΔ.

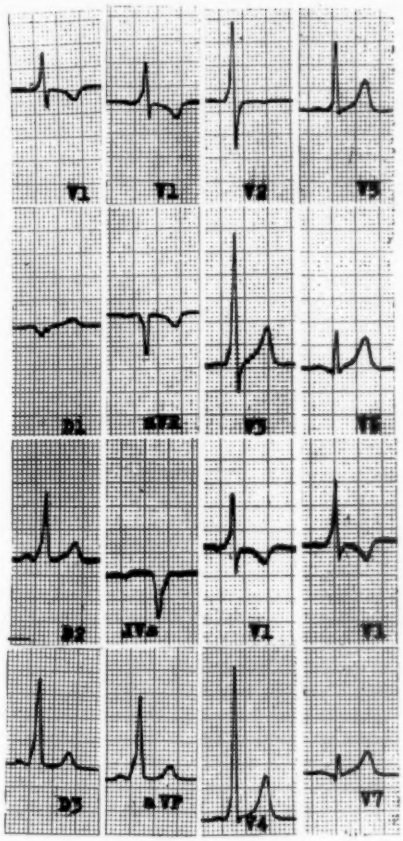

FIG. 7. Case 19. WPW syndrome, type I, in a normal person. Positive T wave from leads V_3 to V_7. Q waves in leads V_6 and V_7, simultaneously registered with delta waves in leads V_1 and V_5.

SUMMARY

A vectorial analysis of twenty-seven electrocardiograms showing the Wolff-Parkinson-White syndrome found among 31,822 (0.085 per cent) tracings was made.

By taking into consideration the delta wave vector orientation (SÂΔ) the cases were classified in two types: 1. WPW syndrome, type I, showing positive delta waves in lead V_2 (SÂΔ with a forward orientation) with SÂQRS pointing either forward or backward; and 2. WPW syndrome, type II, characterized by a negative pre-excitation component in lead V_2 (SÂΔ oriented backward).

Based upon previously published experimental studies and considering the spatial orientation of the SÂΔ, we believe that the area of pre-excitation is probably located at the posterior septal and ventricular regions in the WPW syndrome, type I and at the right and anterior sites

of the interventricular septum and right ventricle in cases of the WPW syndrome, type II.

The average of the spatial angle between SÂQRS and SÂΔ showed a small magnitude (34.7 degrees), with a minimum angle of 10 degrees and a maximum angle of 90 degrees. This finding suggests that the electrical forces developed during the premature excitation may influence the orientation of the total ventricular activation.

Five of six patients showing the WPW syndrome, type I, with large S waves in leads V_1 and V_2, were associated with left ventricular hypertrophy.

Nine of eleven patients presenting positive T waves not opposed to the ventricular complexes in the left precordial leads had normal hearts; but all patients whose electrocardiograms showed negative T waves in leads V_6 and V_7 presented cardiopathies with left ventricular overloading.

Finally, we call attention to the possibility of having the WPW syndrome with Q waves in leads V_6 and V_7 related to a particular orientation of SÂΔ.

Acknowledgments

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References

1. Wolff, L., Parkinson, J. and White, P. D. Bundle branch block with short P-R interval in young people prone to paroxysmal tachycardia. *Am. Heart J.*, 5: 685, 1930.
2. Pearson, J. R. and Wallace, A. B. The syndrome of paroxysmal tachycardia with short P-R interval and prolonged QRS complex. *Ann. Int. Med.*, 2: 830, 1944.
3. Langendorf, R., Lev, M. and Pick, R. Auricular fibrillation with anomalous A-V conduction (W.P.W. syndrome) imitating ventricular paroxysmal tachycardia. A case report with clinical and anatomic findings, and critical review of the literature. *Acta cardiol.*, 7: 241, 1952.
4. Sodi-Pallares, D. New Bases of Electrocardiography. London, 1956. Henry Kimpton.
5. Martins de Oliveira, J., Mendelsohn, D., Nogueira, C. and Zimmerman, H. A. Wolff-Parkinson-White syndrome and tetralogy of Fallot. Report of a case. *Am. J. Cardiol.*, 2: 111, 1958.
6. Ohnell, R. F. Pre-excitation; a cardiac abnormality. *Acta med. Scandinav.* (supp.), p. 152, 1944.
7. Franco, R. J., Villamil, A. and Buzzi, R. M. Consideraciones acerca de la patogenia del sindrome de P-R corto con QRS ancho y mellado. *Semana méd.*, 26: 1257, 1956.
8. Panel Discussion: Anomalous atrioventricular excitation. Symposium on the electrophysiology of the heart. *Ann. New York Acad. Sc.*, 65: 826, 1957.
9. Schafer, H. The general order of excitation and of recovery. Symposium on the electrophysiology of the heart. *Ann. New York Acad. Sc.*, 65: 743, 1957.
10. Sodi-Pallares, D., Bisteni, A., Medrano, G. A., Pileggi, F. and Broncato, R. W. New ideas about the Wolff-Parkinson-White syndrome. To be published.
11. Grishman, A. and Jaffe, H. L. Spatial vectorcardiography—wide QRS complexes with short P-R interval (the Wolff-Parkinson-White syndrome). *J. Mt. Sinai Hosp. New York*, 18: 208, 1951.
12. Odier, J., Montouchet, M. and Dochosal, P. W. Etude spatiale de la composante premature dans le syndrome de Wolff-Parkinson-White. *Cardiologia*, 30: 182, 1957.
13. Genohorsky, J. A vector analysis of the W.P.W. syndrome. *Cardiologia*, 29: 278, 1956.
14. Penaloza, D. and Tranchesi, J. The three main vectors of the ventricular activation process in the normal human heart. *Am. Heart J.*, 49: 51, 1955.
15. Lepeschkin, E. Modern Electrocardiography, vol. 1. Baltimore, 1951. Williams & Wilkins Co.
16. Sodi-Pallares, D., Bisteni, A. and Medrano, G. A. Estudios sobre el sindrome de Wolff-Parkinson-White. Parte 1. La activation ventricular en el sindrome W.P.W. *Arch. Inst. cardiol. Mexico*, 25: 676, 1955.

Wolff-Parkinson-White Syndrome

Report of a Case with Several Types of P Waves, Varying QRS Contour and A-V Nodal Rhythm with Dissociation*

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Since Wolff, Parkinson and White[1] first described the syndrome of short P-R interval and wide, aberrant QRS complex, several theories have been evolved to explain its mechanism which, however, still remains disputed. The purpose of this paper is to report a case in which the electrocardiograms showed several features of interest, some of which may be helpful in understanding the mechanism of the Wolff, Parkinson and White (WPW) syndrome.

Case History

A twenty year old youth was admitted for rheumatoid arthritis of three months' duration. On examination the pulse rate was 60 per minute, the blood pressure 105/60 mm. Hg and a soft systolic murmur was heard at the mitral area. Roentgenogram of the chest showed a normal-sized heart. A routine electrocardiogram showed complexes characteristic of WPW syndrome (Fig. 1). The patient denied any history of paroxysms of tachycardia, and none occurred during his hospital stay of ten weeks.

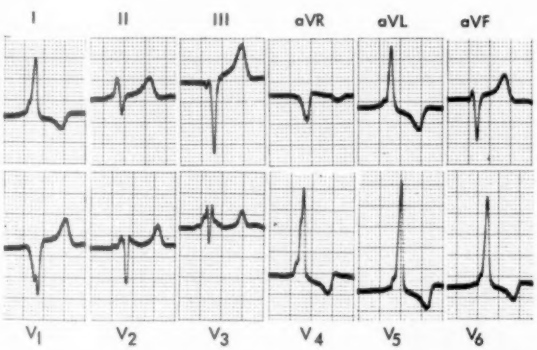

Fig. 1. The dominant WPW complexes (type B) with sinus rhythm seen in this case on most occasions. The P-Δ, QRS and P-S intervals are 0.10, 0.12 and 0.22 second, respectively. The sinus rate varied between 58 and 64 per minute.

Electrocardiograms taken on several occasions showed variations of QRS contour, and on two occasions, A-V nodal rhythm with dissociation. These are illustrated in Figures 2 to 6. The changes in the QRS contour were best seen in lead II and records were therefore taken of this lead (Figs. 3–6).

Comment

Changes in P waves in connection with the WPW syndrome have been commented upon.[2–6] Occurrence of the pre-excitation syndrome only after abnormally formed P waves was reported by Hunter and co-workers.[2] Wolferth and Wood[3] were, however, unable to substantiate the statement that a change occurs in P waves, and found that the contour of the P waves in these cases is remarkably constant when the

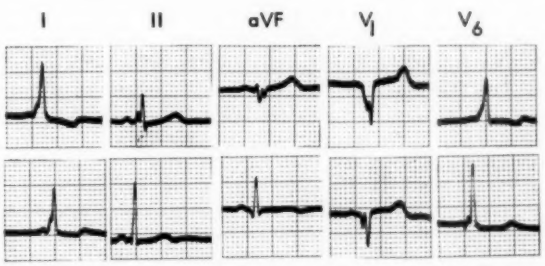

Fig. 2. *Top*, record taken after injection of atropine, $^1/_{100}$ gr. intravenously; the P-Δ, P-R′ (summit of R or R′) and P-S intervals are 0.08, 0.16 and 0.20 second, respectively. *Bottom*, record taken after Master's exercise test; the P-Δ, P-R′ and P-S intervals are 0.08, 0.15 and 0.18 second, respectively. These two records, when compared with Figure 1, show alterations in the QRS contour. The P-Δ interval remains the same while the P-R′ and the P-S intervals shorten. This indicates that atropine and exercise cause accelerated conduction of the sinus impulse via the normal pathway which is responsible for the changes in the QRS contour. This change is best seen in lead II. The negativity of the QRS in V_1 indicates the same type B complexes and rules out the possibility of a second anomalous pathway.

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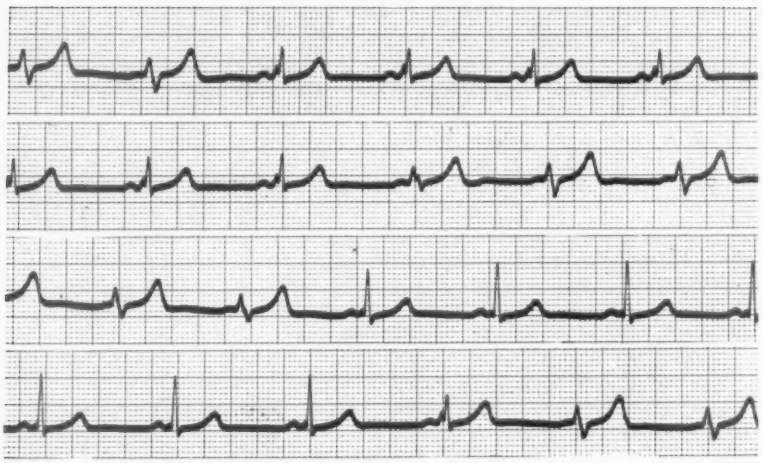

FIG. 3. The four strips are a continuous record of lead II. There is sinus arrhythmia with the sinus rate varying between 58 and 64 per minute. Several different types of P waves are seen; some being low and shallow and others taller and rounded. The QRS contour has no relation to the shape of the P wave; it is the same in several beats with different types of P waves while it varies in other beats with the same types of P waves. In beats with the low shallow type of P wave the P-Δ and P-S intervals are 0.08 and 0.20 second, respectively. The QRS contour varies considerably in other beats. The P-S and the P-R′ (second R peak) intervals, however, are the same, 0.22 and 0.18 second, respectively, in each beat, showing that the impulse is conducted normally via the normal A-V nodal pathway. The P-Δ interval varies between 0.10 and 0.12 second. The last three beats in strip 3 and the first four in strip 4, in which the earliest fraction of the delta wave is just visible, represent minimal fusion and other beats show varying degrees of fusion between the sinus impulse traversing the anomalous and the normal pathways.

ventricular complexes change their shape. Rosenbaum and co-workers[4] noted different types of P waves, nodal and sinus, in a patient showing A-V nodal rhythm. Segers[5] noted, in electrocardiograms of a patient and in experiments on the isolated rabbit heart, two different types of P waves, only one of which was followed by abnormal ventricular complexes after a short P-R interval. Fisch and co-workers[6] noted variation of the P wave with changes in the P-S interval occurring when the heart rate abruptly slowed. Our case clearly depicts the changes in the shape of the P waves which, however, occur irrespective of change in the sinus rate, and which have no definite relation to the QRS contour.

In Figure 3 the QRS contour is seen to vary considerably in different beats. The P-Δ interval lengthens in beats with more normal QRS complexes at the expense of the later fraction of the delta wave. Fisch and co-workers[6] noted prolongation of the P-Δ interval with shortening of the P-S and QRS intervals when the shape of the P wave changed, and suggested that it was due to shift in the pacemaker toward the node and away from the bypass and acceleration of

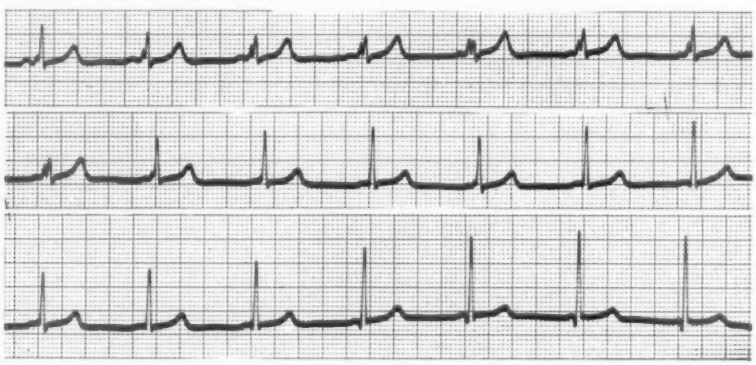

FIG. 4. The three strips are a continuous record of lead II. Beats 1 to 9 are WPW beats with sinus rhythm. The subsequent beats show A-V nodal rhythm with dissociation. Note that the WPW conduction disappears during the nodal rhythm and the QRS becomes of normal duration.

conduction through the A-V node. In our case, however, in beats with a shallow P wave the P-Δ as well as the P-S intervals shortened, suggesting that the pacemaker has shifted toward the node and nearer the origin of the anomalous path. In other beats prolongation of the P-Δ interval occurs irrespective of any change in the shape of P wave (Fig. 3) and the P-S and P-R′ intervals remain unaltered. This clearly shows that this is due to delay in conduction of the sinus impulse in the anomalous pathway while conduction along the normal A-V nodal pathway remains normal, and the variation in the QRS contour is due to variable conductivity of the anomalous pathway. This finding has an important bearing on the origin of the WPW syndrome. It strongly supports the concept of an accessory pathway, and rules out the concept of irritable ventricular focus as there is no reason why the ventricular activation should be delayed.

In addition to the changes in the P waves and the QRS contour seen in Figure 3, the record in Figure 4 illustrates: (1) fusion of two supraventricular impulses, sinus and nodal, in the ventricles, and (2) A-V nodal rhythm with dissociation. There is a series of complexes (beats 10 to 19) with shorter P-S interval and more normal QRS. Some of them show the earliest fraction of the delta wave. There are two alternative explanations for these beats: (1) accelerated conduction along the normal pathway or (2) escape of an ectopic pacemaker in the A-V node with fusion of two supraventricular impulses, the sinus impulse conducted along the anomalous path and the nodal impulse conducted along the normal path. It is most unlikely for acceleration of as much as 0.06 second to occur in the normal path spontaneously. Again these beats are immediately followed by A-V nodal rhythm with dissociation. There is, therefore, little doubt that these beats represent fusion of two supraventricular impulses. Such complexes, intermediate in form between those characteristic of sinus rhythm and those characteristic of A-V rhythm, have been noted to occur during transition from sinus to A-V nodal rhythm in patients with the WPW syndrome and ascribed to fusion of two supraventricular impulses.[4,7,8] In these beats the retrograde conduction of the nodal beat is blocked below the origin of the anomalous path.

Conduction of the sinus impulse along the

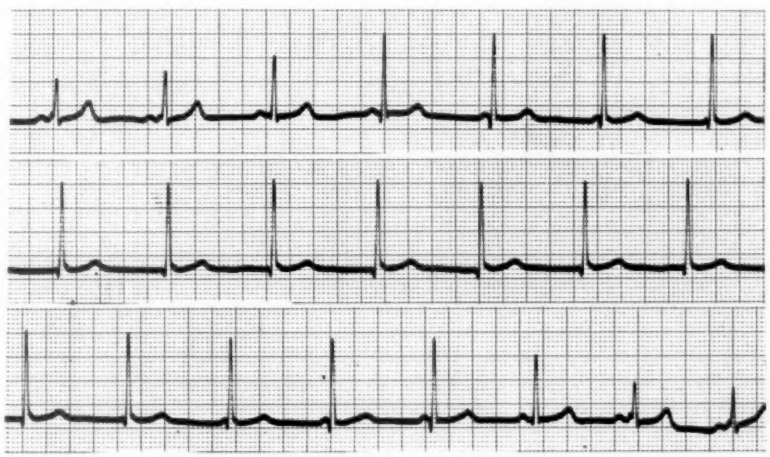

FIG. 5. The three strips are a continuous record of lead II. In the top strip an initial delta wave is seen in the first two beats; it is hardly visible in the third beat, and is absent in the fourth beat. Thereafter A-V nodal rhythm with dissociation is seen, which continues until the last two beats in the lowest strip. The third and fourth beats of the top strip represent fusion of two supraventricular impulses as described in Figure 4. From the third to seventh beat the RR or the internodal interval is 0.92 second while the PP interval gradually lengthens from 0.92 to 0.96 second with slowing of the sinus rate. The nodal QRS appears with increasing prematurity and is superimposed on the gradually shortening portion of the sinus P wave. In the middle strip the P wave is absent; either it is buried in the QRS or there is atrial standstill. Atrial standstill in this syndrome had been noted during A-V rhythm after quinidine administration.[6] In the bottom strip the P wave reappears in the second beat. The internodal interval further shortens to 0.83 second in the sixth beat. The PP interval gradually decreases from 0.86 to 0.83 in the sixth beat. The sinus rate is, however, faster than the nodal rate; more and more of the P wave precedes the nodal QRS in each succeeding beat till the sinus impulse is first conducted along the anomalous pathway and then along both the pathways with termination of A-V rhythm.

anomalous pathway in the presence of nodal rhythm strongly supports the concept of a structural anomaly of the accessory pathway. Accelerated conduction in the A-V node itself due to longitudinal functional dissociation[9] is unlikely in the presence of impulses arising within the node itself.

A-V rhythm and dissociation is usually seen in the WPW syndrome during maneuvers like carotid sinus pressure or other types of vagal stimulation applied for experimental reasons or to break the paroxysm of tachycardia.[10] In our case the ectopic rhythm appeared spontaneously, apparently due to partial and asynchronous release of the A-V node from the influence of the vagus nerve while the sinus node is still under its control.[11] The absence of a delta wave in beats with A-V rhythm with dissociation shows that the sinus and the nodal impulses interfere with each other either above, within or at the ventricular end of the anomalous pathway.[10]

Figure 5 shows rapid transition from WPW conduction to fusion of two supraventricular impulses and then to A-V rhythm with dissociation and vice versa. Dissociation occurs when the sinus rate slows slightly and is terminated when it becomes slightly faster than the nodal rate.

Measurement of the duration of the P wave preceding the nodal QRS complexes in Figures 4 and 5 shows that when this duration is less than 0.08 second there is no fusion of the sinus and nodal impulses, and A-V dissociation appears. This shows that the ventricular activation through the anomalous pathway is impossible when the nodal activation occurs less than 0.08 second after the sinus impulse.

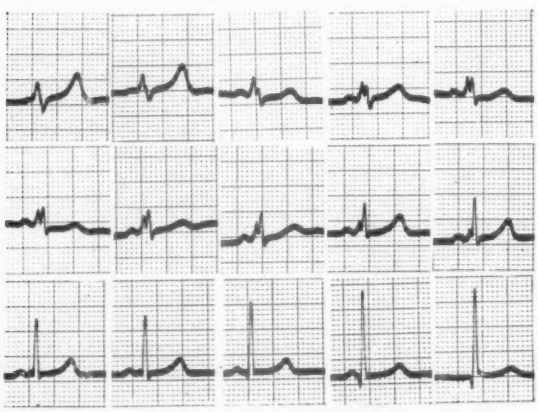

FIG. 6. A collection of individual beats cut from a continuous strip and rearranged to show all stages of fine transitions from the dominant WPW type of QRS complex to the ectopic nodal complex. These beats also show the various features described in previous figures. Beats 1 to 12 are WPW beats with sinus rhythm, beats 13 and 14 represent fusion of nodal and sinus impulses, and the last beat is a pure nodal complex.

SUMMARY

The present case illustrates: (1) Shifting sinus pacemaker with several different types of P waves irrespective of the sinus rate; (2) absence of relation between the type of the P wave and the QRS contour; (3) prolongation of the P-Δ interval at the expense of the later fraction of the delta wave and varying QRS contour in WPW beats as a result of varying conductivity of the anomalous pathway; (4) fusion of two supraventricular impulses, the sinus impulse traversing the anomalous path and the nodal impulse the normal path; and (5) A-V nodal rhythm with dissociation. Some of the findings in this case strongly support the hypothesis of a structural anomaly of the accessory pathway.

ACKNOWLEDGMENT

Dr. L. R. Sarin, Superintendent, Sawai Man Singh Hospital, kindly permitted the publication of this report.

REFERENCES

1. WOLFF, L., PARKINSON, J. and WHITE, P. D. Bundle branch block with short P-R interval in healthy young people prone to paroxysmal tachycardia. *Am. Heart J.*, 5: 685, 1930.
2. HUNTER, A., PAPP, C. and PARKINSON, J. The syndrome of short P-R interval, apparent bundle branch block, and associated paroxysmal tachycardia. *Brit. Heart J.*, 2: 107, 1940.
3. WOLFERTH, C. C. and WOOD, F. C. Further observations on the mechanism of production of a short P-R interval in association with prolongation of the QRS complex. *Am. Heart J.*, 22: 450, 1941.
4. ROSENBAUM, F. F., HECHT, H. H., WILSON, F. N. and JOHNSTON, F. D. The potential variations of the thorax and the esophagus in anomalous atrioventricular excitation (Wolff-Parkinson-White syndrome). *Am. Heart J.*, 29: 281, 1945.
5. SEGERS, M. La synchronisation auriculo-ventriculaire et le syndrome de Wolff-Parkinson-White. *Arch. mal. coeur*, 44: 712, 1951. Cited by SCHERF, D., BLUMENFELD, S. and MUELLER, P. A-V conduction disturbance in the presence of the preexcitation syndrome. *Am. Heart J.*, 43: 829, 1952.
6. FISCH, C., PINSKY, S. T. and SHIELDS, J. P. Wolff-Parkinson-White syndrome. Report of a case associated with wandering pacemaker, atrial tachycardia, atrial fibrillation, and incomplete A-V dissociation with interference. *Circulation*, 16: 1004, 1957.

7. MALLINOW, M. R. and LANGENDORF, R. Different mechanisms of fusion beats. *Am. Heart J.*, 35: 449, 1948.

8 MILLER, R. and SHARRETT, R. H. Interference dissociation. *Circulation*, 16: 803, 1957.

9. PRINZMETAL, M., KENNAMER, R., CORDAY, E., OSBORNE, J. M., FIELDS, J. and SMITH, L. A. Accelerated Conduction: The Wolff-Parkinson-White Syndrome and Related Conditions. New York, 1952. Grune & Stratton.

10. KATZ, L. N. and PICK, A. Clinical Electrocardiography. I. The Arrhythmias. Philadelphia, 1956. Lea & Febiger.

11 FOX, T. T., TRAVELL, J. and MOLOFSKY, L. Action of digitalis on conduction in the syndrome of short P-R interval and prolonged QRS complex. *Arch. Int. Med.*, 71: 206, 1943.

Multiple Variations of WPW Conduction in One Subject

Intermittent Normal Conduction and a False Positive Exercise Tolerance Test*

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THE purpose of this report is to point up the variations in conduction which may occur in the presence of the Wolff-Parkinson-White syndrome. An unusual case is used to illustrate the pitfalls that may occur if these variations are not appreciated. In this particular case, ST segment changes lead to an erroneous interpretation of a positive exercise test.

CASE HISTORY

This forty-one year old officer had his first electrocardiogram in April 1956 (Fig. 1A). It was noted to be abnormal but the nature of the abnormality was not recognized by the attending physician. It was considered that the patient possibly had arteriosclerotic heart disease. He was asked to reduce his weight and limit his fat intake. In November 1956, his ECG was repeated (Fig. 1B). It was noted to be quite different from the earlier tracing. It was elected to do a single Master's exercise tolerance test. Following exertion there was segmental ST segment depression particularly over the left precordium (Fig. 1C). For this reason the record was interpreted as a positive exercise tolerance test. However, careful attention indicates an early QRS activation, well noted in lead II, at the expense of the P-R interval. The rate was not significantly changed after exercise and there were no symptoms during exertion.

During the period of observation the patient remained asymptomatic. His family history revealed longevity with both grandfathers living beyond eighty years of age. The patient was seen in consultation at the School of Aviation Medicine in April 1957. On physical examina-

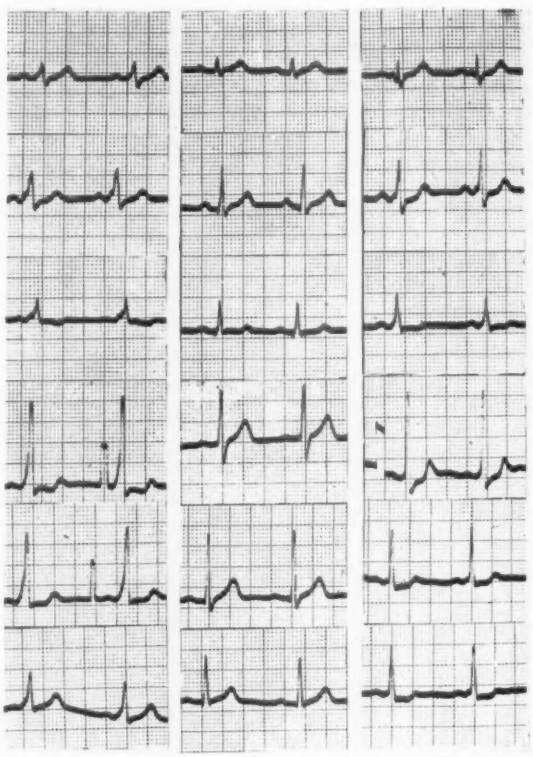

FIG. 1. A, The initial electrocardiogram recorded during an annual physical examination shows a typical WPW record. B, the second electrocardiogram recorded six months later is entirely normal. C, immediately after exercise ST segment depression is noted in leads II, III, V_4, V_5 and V_6. There is evidence of early excitation in the P-R segment. Even though the P-R segment is shortened compared to normal conduction it is still greater than 0.12 second. This is a form of accelerated conduction, another variant of WPW type conduction, with secondary ST segment and T wave changes.

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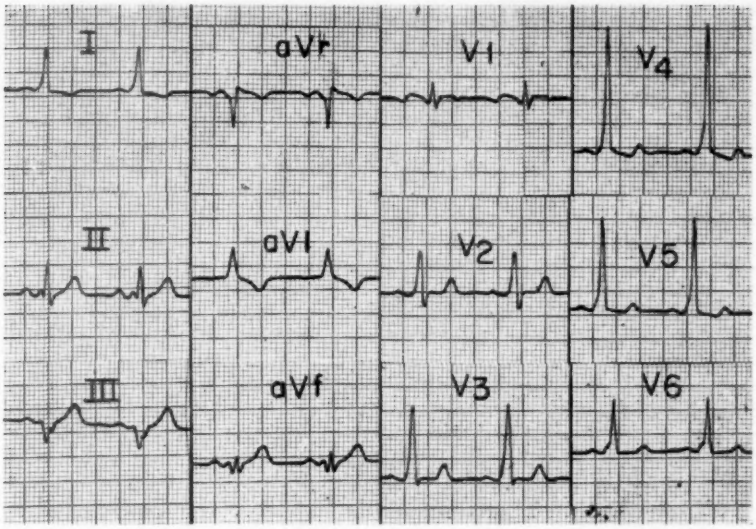


FIG. 2. This is a complete electrocardiogram demonstrating one variation of the WPW syndrome in this case. Note the P-R interval is 0.14 second and the QRS duration is 0.16 second (lead II). The P-R interval in the normal record was 0.20 second and the QRS duration 0.11 second (Fig. 6). The pre-excitation wave in lead II is a distinct initial R wave occurring during the normal time of the P-R segment. This is sometimes called an X wave.

tion no significant abnormalities were apparent.

Laboratory Studies: Hemogram, normal; sedimentation rate, 12 mm.; fasting blood sugar, 100 mg. per cent; urinalysis, normal; serology, negative. The S_f studies were as follows: S_f 0–12, 383 mg./100 ml.; 12–20, 40 mg. per cent; 20–400, 66 mg./100 ml.; atherogenic index, 57; the blood cholesterol was 273 mg./100 ml. with a phospholipid/cholesterol ratio of 0.92. The chest x-ray was normal.

ECG Findings: The electrocardiographic examination on the first visit to the Internal Medicine Department demonstrated two different types of Wolff-Parkinson-White conduction. One or the other of these two types of conduction was persistently present without intermediate forms (Figs. 2 and 3). Previous experience indicated that WPW conduction can be profoundly altered by respiration;[1] accordingly, breathing maneuvers were performed. At the height of inspiration a normally conducted beat was recorded (Fig. 4). Still a third type of WPW conduction was noted immediately preceding and immediately after the normally conducted beat. The conversion to normal conduction was again accomplished with successful maintenance of normal conduction at the height of inspiration for four successive cycles.

The following day the patient was studied again. The initial record was entirely normal (Fig. 5). Following a series of respiratory maneuvers, WPW conduction became evident. During this examination seven new variations in WPW conduction were demonstrated (Figs. 6 and 7). By recording simultaneous leads the possibility of positional changes was excluded. One variation was identical to the initial record of April 1956. Within two days ten different

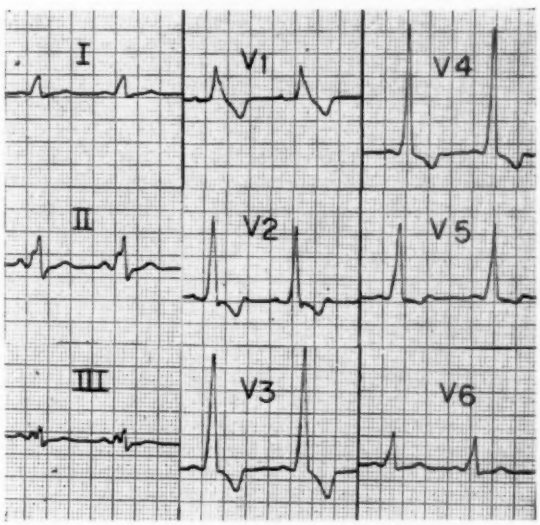


FIG. 3. This is the electrocardiogram of a second variant of WPW conduction. The P-R interval is shortened to the classic 0.10 second time interval.

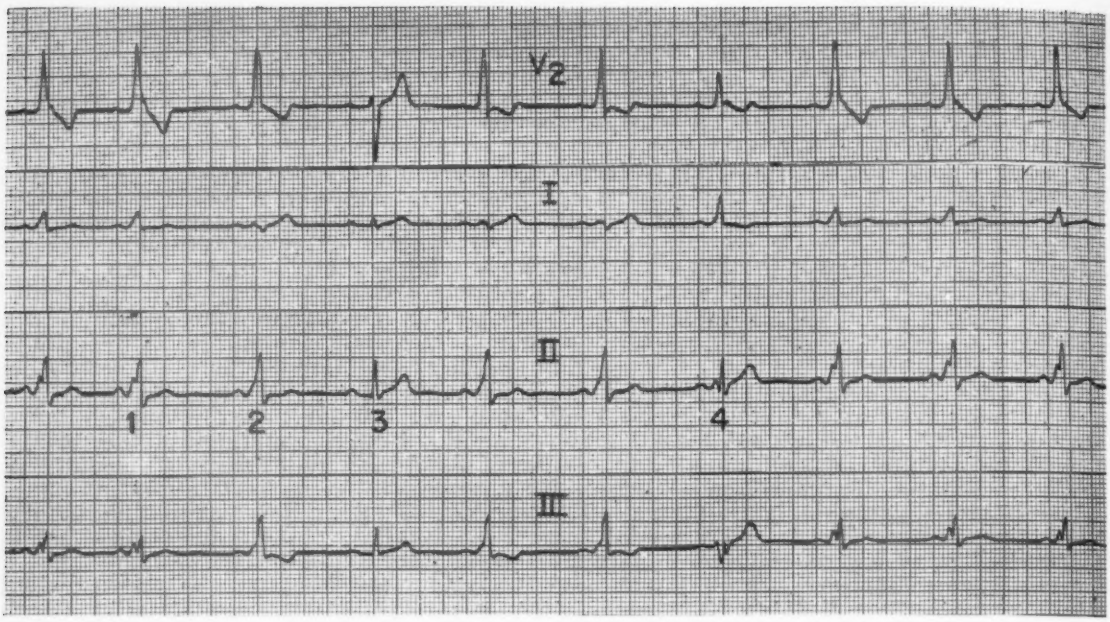


FIG. 4. This is a continuous simultaneous recording demonstrating four forms of ventricular conduction in a short interval. The subject holds his breath at the height of deep inspiration at the time of the normally conducted cycle (3). Note the characteristic of the complex (2) preceding and following the normally conducted cycle. Numbers 1 and 4 identify the other two variants.

variations in ventricular excitation of the WPW type were noted as well as normal conduction.

COMMENT

This case demonstrates the extreme of variability in ventricular conduction with secondary recovery changes of the ST segment and T wave that may be encountered in the WPW syndrome. It is important to recognize that more than one form of ventricular excitation can exist in the same individual with a WPW syndrome. These variations are not to be confused with a wandering pacemaker. The S-A node initiated the impulse in all instances noted in this case. While it is more common to see one persistent characteristic WPW pattern in a patient, it is clear that multiple forms of excitation can and do occur in the same individual. None of the variations in conduction were associated with arrhythmia.

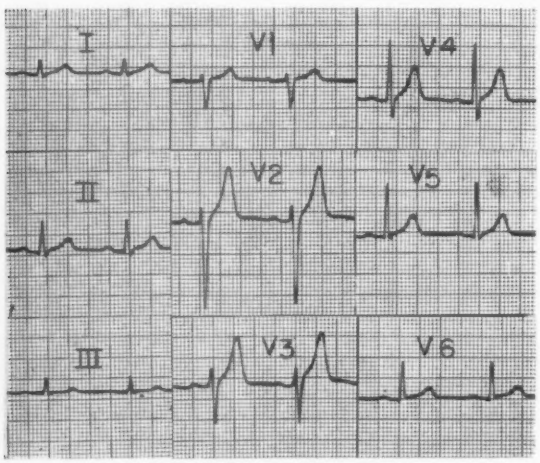


FIG. 5. This is a normal electrocardiogram. The P-R interval is 0.20 second and the QRS duration is 0.11 second. Some divergence of opinion could be expressed regarding the QRS duration. However, the borderline prolongation is of no clinical significance.

Another important facet of the WPW syndrome is pointed up in this case—ST segment and T wave changes secondary to an abnormality in excitation. This fact, not coronary insufficiency, accounts for the ST segment changes noted after exercise. When the normal order of ventricular excitation occurred the ST segment and T waves were quite normal. ST segment and T wave changes noted in the presence of WPW syndrome cannot be attributed to cardiac disease.

Intermittent recording of normal records in examples of WPW syndrome causes much confusion. They are not indicative of any important changes in cardiac status.

This case, like many others that are detected during examination for reasons other than vol-

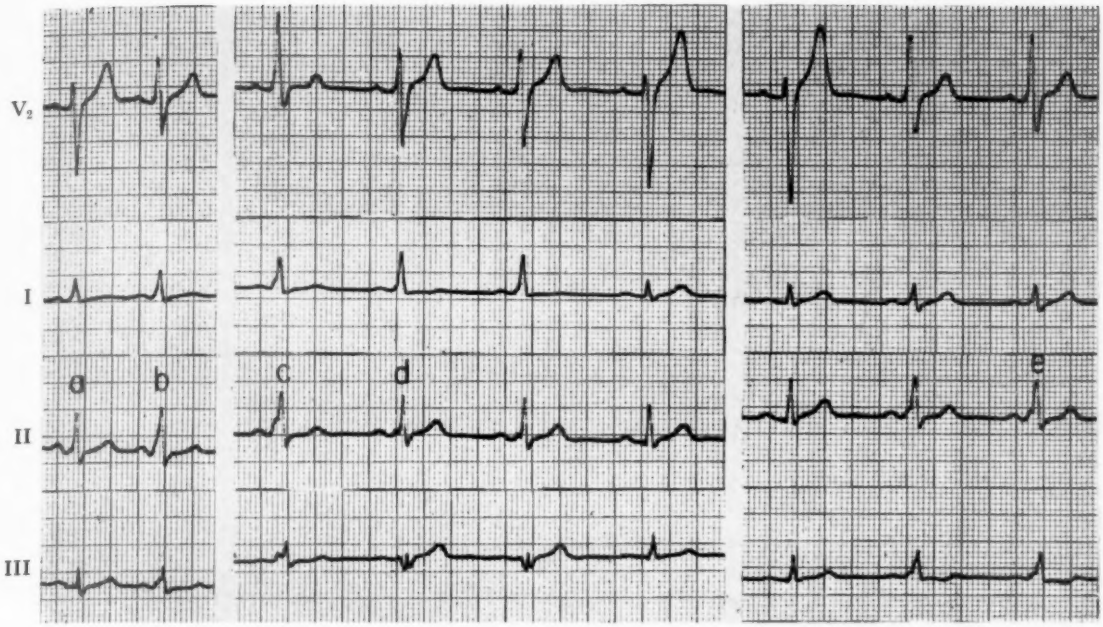


FIG. 6. This record demonstrates five additional variants in WPW conduction (a, b, c, d and e). Normal complexes are seen in the second complex following type *d*. The following strip of normal cycles has been removed.

untary consultation with the physician, had no evidence of arrhythmia or paroxysmal tachycardia. The true incidence of paroxysmal tachycardia in the WPW syndrome will not be known until a series from a nonpatient population is studied.

In this case several of the variants with distinct pre-excitation waves had P-R intervals greater than 0.10 second. In one variant the P-R interval was noted to be 0.14 second with a definite form of pre-excitation (Fig. 2). In other variants the P-R interval is the classic 0.10

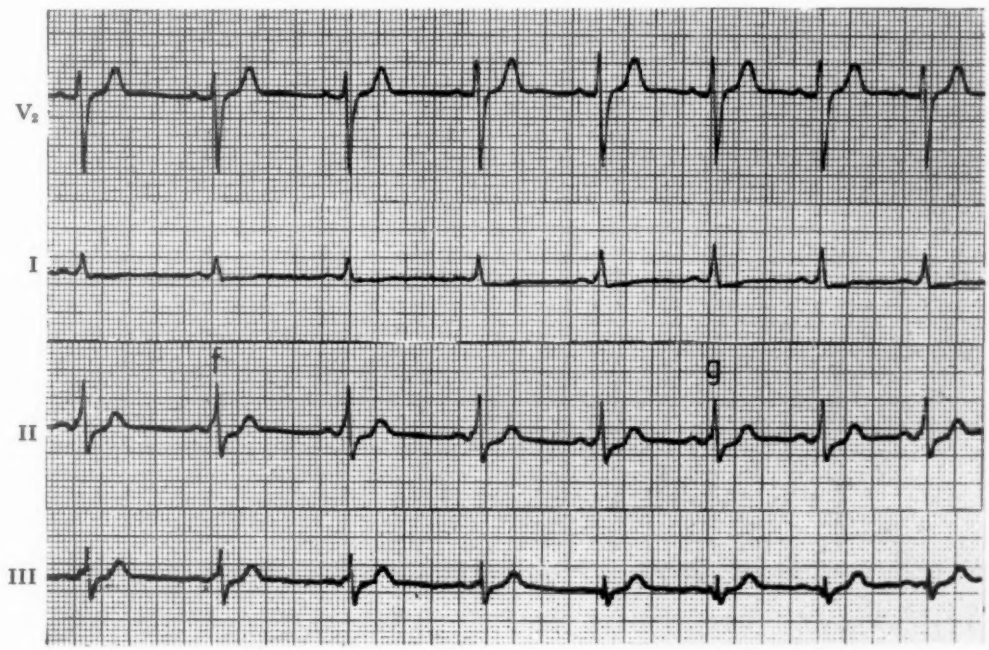
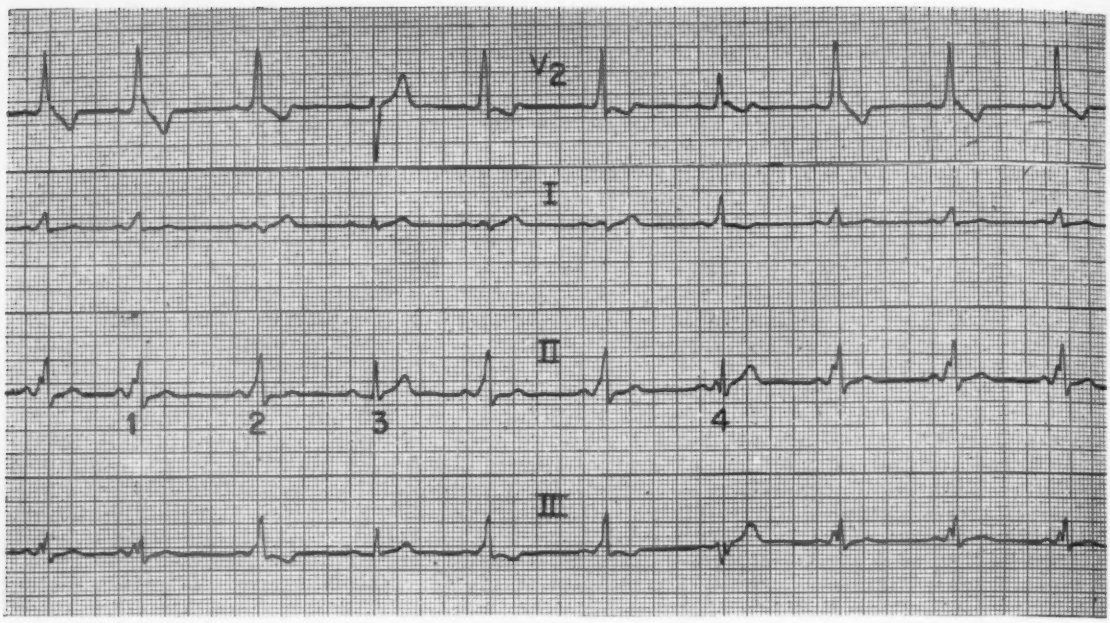


FIG. 7. Two additional variations of conduction are seen in this portion of the record (f and g).



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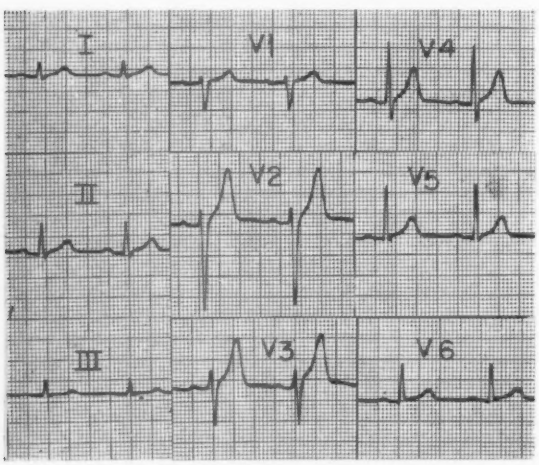

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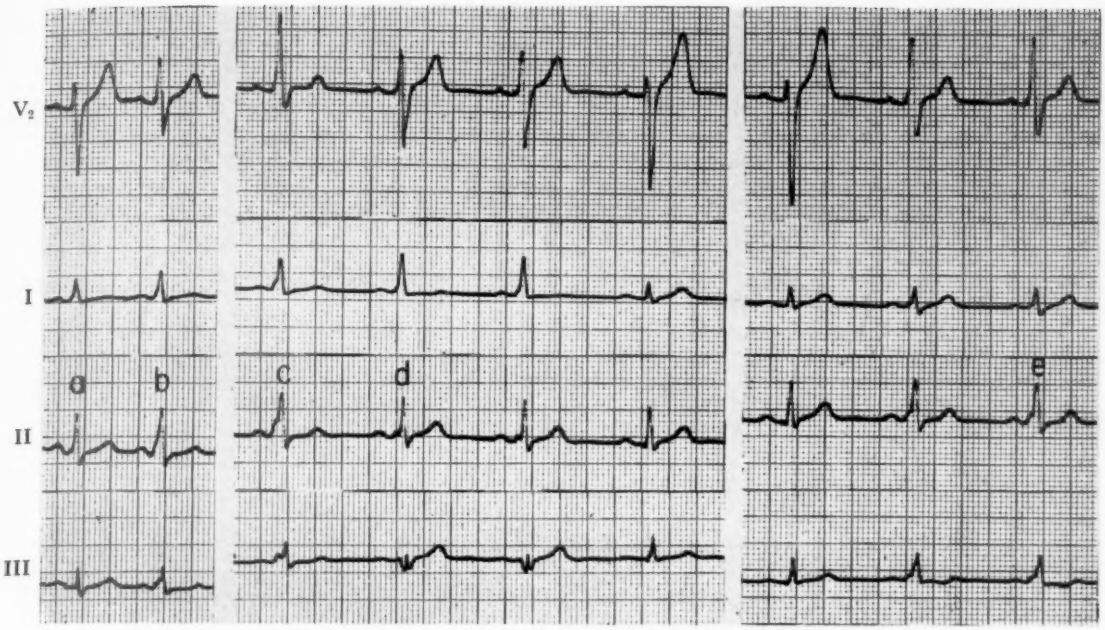

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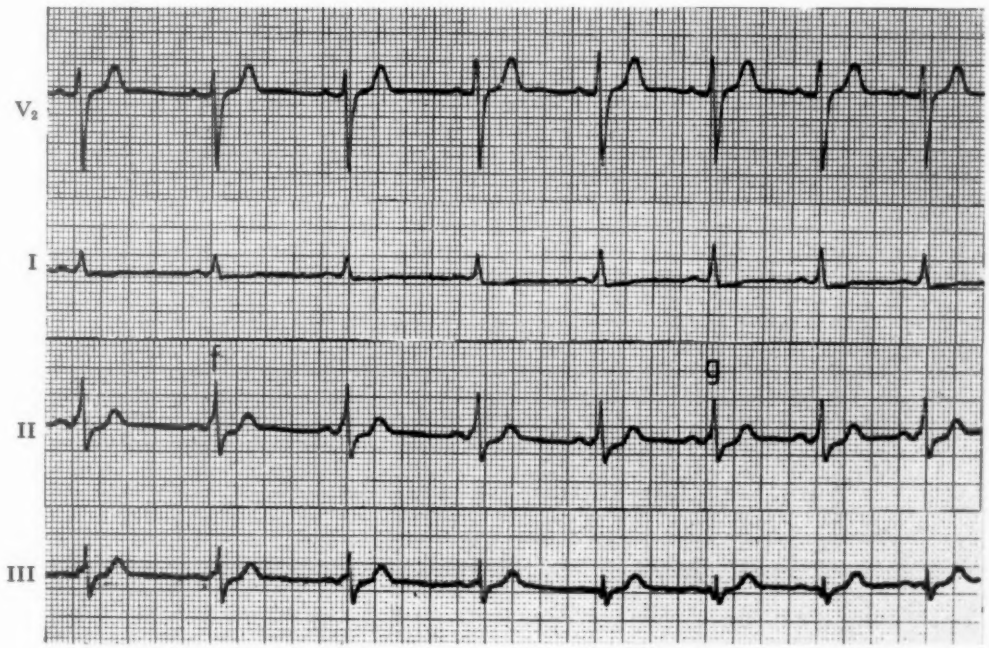

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second interval (Fig. 3). This raises a serious question as to the advisability of using a set time value for the P-R interval in examples of the WPW syndrome. In this case the shortening of the P-R interval due to the increase in the QRS duration as compared to the patient's normal record is the real diagnostic clue.

The role of respiration in producing WPW conduction or converting WPW conduction to normal has been reported elsewhere.[1] This is again demonstrated in this case.

Summary

A case is presented demonstrating a number of important facets of the WPW syndrome:

(1) Multiple variation in ventricular excitation; (2) intermittent normal electrocardiograms; (3) variations in the P-R interval with P-R intervals of 0.14 second in the presence of pre-excitation; (4) ST segment and T wave changes secondary to pre-excitation (this leads to a false impression of a positive exercise tolerance test); (5) conversion to normal conduction.

No other arrhythmia or indication of underlying cardiac disease was noted.

Reference

1. Lamb, L. E. Respiratory maneuvers in converting WPW syndrome to normal conduction and converting normal conduction to a WPW syndrome. *Am. Heart J.*, 55: 174, 1958.

Symposium on Phonocardiography (III)

The Pericardial Friction Rub in the Phonocardiogram*

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Sound phenomena caused by pathologic alterations of the pericardial sac have been known for a long time. In most cases, the diagnosis of pericarditis is based on the observation of such murmurs. In 1842, Škoda gave a precise description of pericardial friction rubs as they are recognized by the ear.[10] Changes of the auscultatory findings during the course of the disease and the time relationship of the rub with the cardiac cycle were described by him. His classic description is still considered basically correct.[1,3,11,12]

Auscultatory Characteristics of Friction Rubs

The pericardial friction rub, which has an extracardiac origin, should be distinguished from intracardiac murmurs. This is not always possible by auscultation, and errors may occur. Through precise observation, the old clinicians described a series of differential data, and the most important will be briefly mentioned. The auditory character of the pericardial rub is variable: "soft, grating or scratching."[9] The differentiation between extracardiac and intracardiac murmurs is not possible if they occur only in systole, since the acoustical character of systolic murmurs may vary considerably. It is often stated that friction rubs are "more superficial," i.e., closer to the ear, than intracardiac murmurs. However, this is not always true. High-pitched cardiac murmurs may seem close to the ear. The transitoriness of pericardial friction rubs and their observation in sharply localized areas are common, but by no means constant findings. The Valsalva maneuver decreases intracardiac murmurs and may cause their disappearance. On the other hand, we rarely find a definite change of intensity and character of pericardial friction rubs during respiration.

Phonocardiographic Features

In the phonocardiogram, the pericardial friction rub may change considerably in regard to form and timing, even within a few hours. This lack of uniformity is impressive and constant. Rapidly changing pictures are observed, including more or less spindle-like patterns, crescendo or decrescendo groups of vibrations, and even snapping sounds, connected with each other by smaller vibrations. Changes in amplitude are often sudden, from one beat to the next (Figs. 1–6).

It is well known that pericardial friction rubs may occur during systole or diastole, or during both systole and diastole. They may consist of several different phases.

Systolic Rubs: The group of vibrations which occurs during systole may immediately follow the first sound, or it may occur after a short interval, in early systole or mid-systole. Even late systolic murmurs, which either fuse with the second sound or are separated from it, were observed. Vibrations lasting throughout the entire systole with rapidly changing amplitude may also occur (Fig. 2). Finally, sound-like vibrations are found which produce a form of gallop rhythm on auscultation and appear as "clicks" in the phonocardiogram.

Diastolic Rubs: The groups of vibrations which occur during diastole demonstrate qualities

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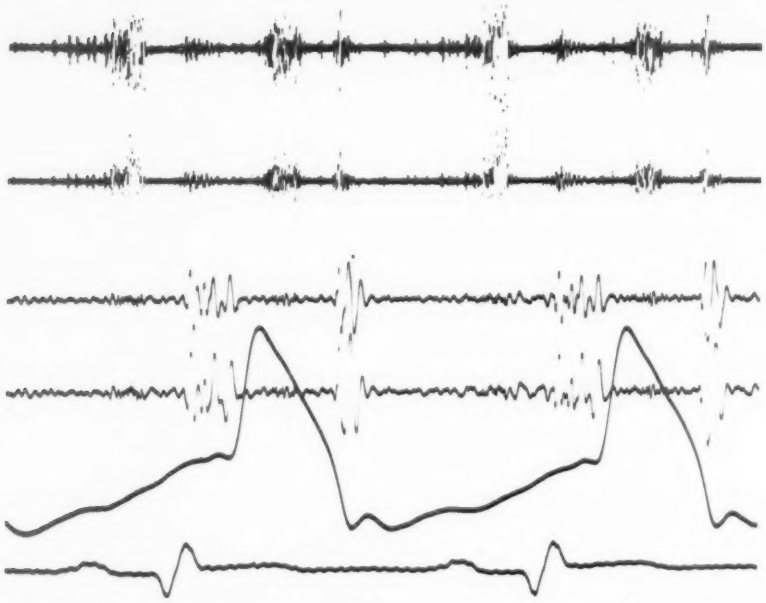

FIG. 1. Phonographic record with the microphone at the tip of the sternum. Paper speed, 100 mm./sec. *Tracings (top down):* phonocardiograms from above at 250, 140, 75 and 35 limits of cut-off; carotid pulse; electrocardiogram (lead II). *Pericardial rub* which extends almost through the entire diastole with variations of amplitude. It ends suddenly with a large oscillation 0.07 second before the beginning of the first sound; therefore, it cannot be confused with a presystolic murmur of mitral stenosis. It also contains some low frequency vibrations. There also is a mid-systolic murmur of variable amplitude which lasts 0.08 second and is demonstrated particularly in the high-pitched curve.

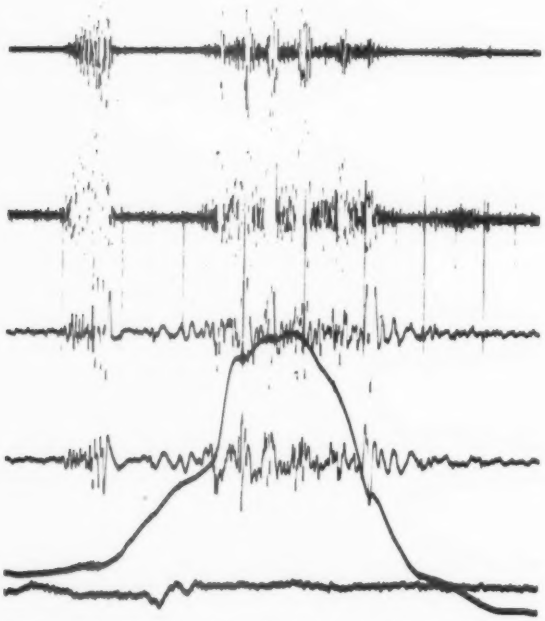

FIG. 2. Microphone placed in the fifth intercostal space at the left sternal border. Other data as in Figure 1. *Pericardial rub* which consists of three parts: (1) A presystolic phase, which starts 0.08 second after the beginning of the P wave, is recorded in all tracings and looks like a sound. (2) An all-systolic murmur, divided in several groups, connected by oscillations of lesser amplitude. (3) An early diastolic rub of small amplitude which starts 0.12 second after the beginning of the second sound and does not contain low frequency vibrations.

similar to those of systole. They may be seen in presystole and in mid- or early diastole. They may immediately follow the second sound or, beginning with great amplitude, follow the second sound after a short interval, so that they give the impression of a split second sound. If there is A-V block, it can be proved that the vibrations which occur in presystole are caused by atrial contraction (Fig. 5). If the atrial contraction is normal, these vibrations coincide with the beginning of the P wave. This early beginning reveals that they do not represent an atrial (fourth) sound or a crescendo murmur caused by mitral stenosis. The presystolic rub may end with the P wave or continue, with low amplitude vibrations, until the beginning of the following first sound. Presystolic crescendo rubs, which continue with the first sound without

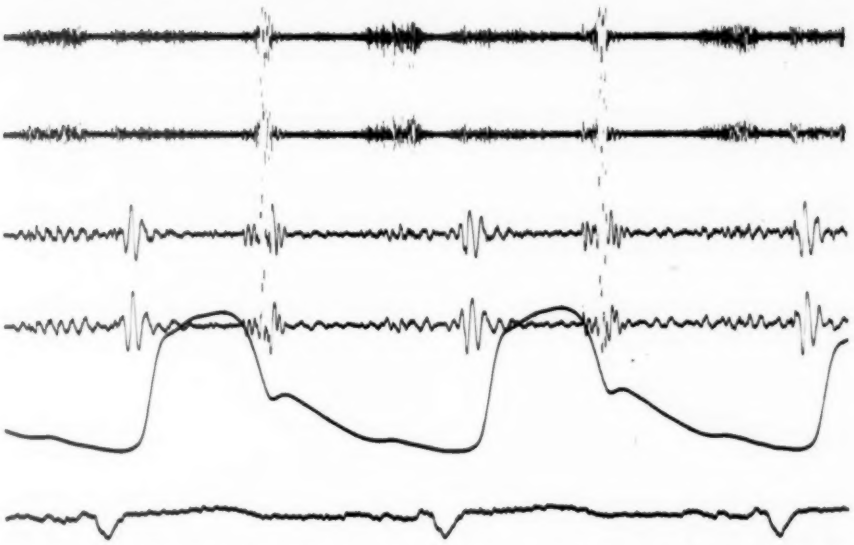

FIG. 3. Microphone in the fifth intercostal space at the left sternal border. Other data as in Figure 1. Record shows that low frequencies also occasionally occur in pericardial friction rubs.

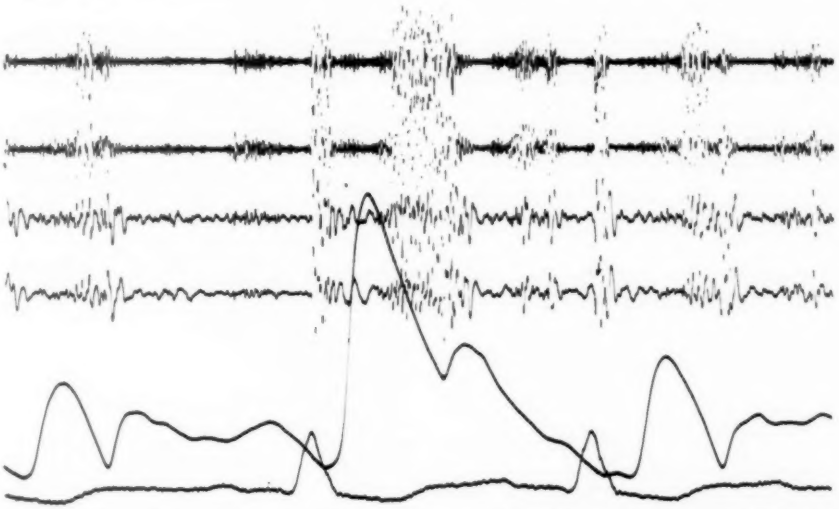

FIG. 4. Microphone at the tip of the sternum. Other data as in Figure 1. *Pleuropericardial friction rub* which contains a presystolic phase beginning with the P wave and ending before the Q wave, and a systolic phase beginning late in systole and extending beyond the second sound. The latter is of great intensity. There is a remarkable change of intensity with varying lengths of the diastoles. During a long diastole, the presystolic phase is small and the following systolic phase is large. The opposite occurs for a short diastole. This is explained by the variable intensity of motion of the atria which performs a smaller contraction when the ventricle is almost completely filled than if it is empty. On the other hand, the ventricular contraction occurring after a prolonged diastolic filling is more powerful. Both rubs disappeared within ten days.

decrease of amplitude, have not been recorded.

Duration: An improvement of the pericarditis is usually accompanied by a decrease in the amplitude of the vibrations recorded by the phonocardiograph. However, such a decrease is not always evidence of improvement.

If the rub consists of several parts, the systolic group is usually the longest. Late systolic murmurs or systolic clicks may continue for weeks, years, or even for the rest of the patient's life.[4,6]

Frequency Characteristics: In the medical litera-

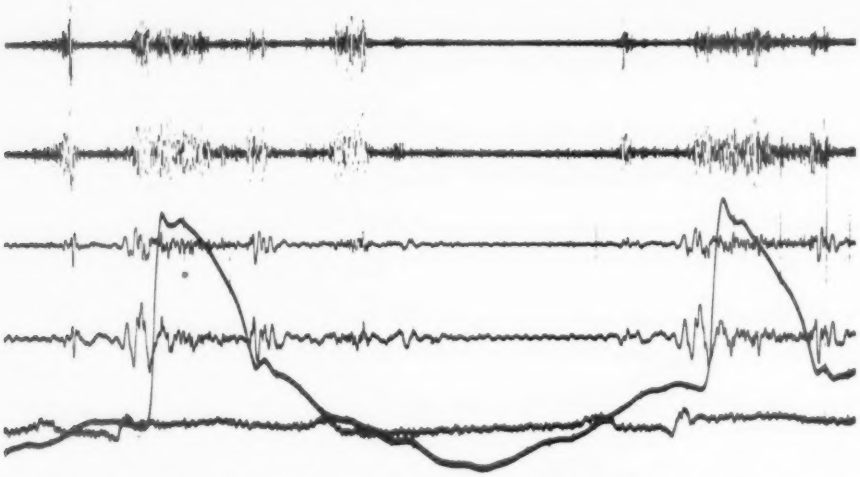

FIG. 5. Microphone in the fifth intercostal space at the left sternal border. Patient with pericarditis following myocardial infarction and A-V block. Three atrial contractions are shown, one before the first QRS complex, one 0.12 second after the incisura of the first arterial pulse and one 0.13 second before the beginning of the second Q wave. The atrial contraction which begins at the onset of diastole and in which the atria are able to contract maximally against the least resistance has the greatest intensity. Figure 2 shows a tracing of the same patient, recorded the following day. The rapid change of the vibrations is demonstrated by comparing the two tracings. The systolic vibrations, which had been considered as of endocardial origin (Fig. 5), were later (Fig. 2) proved to be pericardial because of the irregular shape. The A-V block had disappeared.

ture, pericardial friction rubs are described as being caused by high frequency vibrations.[2,5–8] In our experience, this is usually correct, although there are exceptions. In a certain number of cases, we had the impression that there also were low frequency vibrations, possibly with groups of sinusoidal oscillations, i.e., with the character of a musical murmur. In most cases, however, the frequency of the pericardial friction rub is higher than that of the diastolic murmur of mitral stenosis.

DIFFERENTIAL DIAGNOSIS OF RUBS AND MURMURS

In the following paragraphs, we shall attempt to describe the basic differential features between pericardial rubs and other murmurs which might be confused with them.

1. A pericardial friction rub differs from the rumbling early or mid-diastolic murmur of mitral stenosis by its high frequency.

2. The variability of form and amplitude is in general not observed in mitral stenosis.

3. We have never observed a pericardial presystolic rub which could be confused with the presystolic murmur of mitral stenosis. The latter shows a typical crescendo type (if the PQ interval is normal) and immediately continues into the first sound. This was never observed in patients with pericardial friction rubs. As a rule, there is a brief gap between the rub and the first sound or, if the rub lasts until the beginning of the first sound, its amplitude decreases so that it is not in crescendo.

4. The pericardial presystolic rub frequently begins earlier than the atrial sound or the crescendo murmur of mitral stenosis, i.e., it starts shortly after the onset of the P wave.

5. The diastolic murmur of either organic or functional aortic or pulmonic regurgitation is easily recognized because of the decrescendo character of this murmur. The clinical picture and the usually different localization of the murmur are also of help. As a rule, there is no definite difference in frequency between rubs and aortic diastolic murmurs.

6. It is difficult to differentiate between pericardial rubs and pleuropericardial rubs. The latter have a different origin but are similar in regard to pattern and localization. The course of the disease and other clinical data will have to be relied upon (Fig. 4).

7. The same is true in the differentiation of rubs from organic or functional systolic murmurs. The most reliable data are the fractionation of the pericardial rub and its predominant content of high frequencies.

8. Artefacts should also be mentioned. They occur predominantly in the range of high fre-

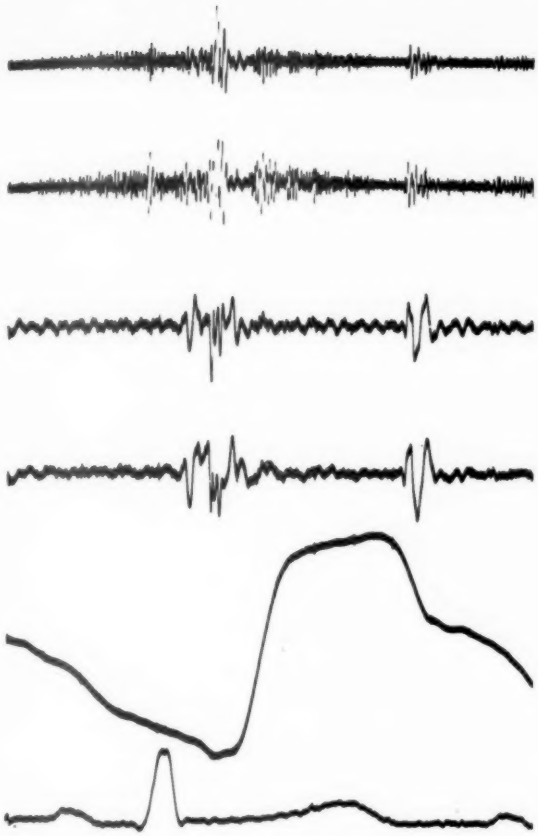

FIG. 6. Data as in Figure 1. This *presystolic pericardial rub* is similar to that of cases of mitral stenosis. It is marked by a slow crescendo with a minor drop of amplitude at the time of the Q wave. The differentiation is possible by the almost simultaneous beginning of the P wave and rub and by the lack of low frequencies.

quencies and may repeat themselves with some regularity in several beats, or in a sequence of beats, if the microphone or its support is set into vibration by motion of the thoracic wall.

SUMMARY

The sound phenomena caused by pericarditis are discussed in regard to their acoustical qualities and their peculiarities, as demonstrated in the phonocardiogram.

1. Pericardial murmurs are predominantly of high frequency, but may also contain vibrations of low frequency.

2. Their amplitude varies considerably.

3. No regularity of pattern or time relationship can be recognized in these rubs. They may appear in any phase of the heart action and may consist of either one or several groups.

4. Presystolic rubs appear earlier than atrial sounds or the presystolic murmur (mitral stenosis). They occur either at or shortly after the onset of the P wave.

5. Using these criteria, endocardial and pericardial vibrations may be distinguished, with few exceptions, by means of the phonocardiogram, even when this is not possible by auscultation.

REFERENCES

1. BLUMER, G. Pericarditis epistenocardica. *J. A. M. A.*, 107: 178, 1936.
2. CALO, X. Les Bruits du Coeur et des Vaisseaux. Paris, 1950. Masson et Cie.
3. FRIEDBERG, C. K. Diseases of the Heart. Philadelphia, 1956. W. B. Saunders Co.
4. GMACHL, E. Über meso- und telesystolische Schallphänomene. *Ztschr. f. Kreislaufforsch.*, 42: 502, 1953.
5. HEGGLIN, R. Differentialdiagnose Innerer Krankheiten. Stuttgart, 1957. Georg Thieme Verlag.
6. HOLLDACK, K. Atlas und kurzgefasstes Lehrbuch der Phonokardiographie. Stuttgart, 1956. Georg Theieme Verlag.
7. JONA, E. et al. Il fonocardiogramma epicardico dell'uomo., *Minerva med.*, 49: 47, 1957.
8. LUISADA, A. A. The Heart Beat. New York, 1953. Paul B. Hoeber, Inc.
9. SAHLI, H. Lehrbuch der klinischen Untersuchungsmethoden. Leipzig und Wien, 1909. Franz Deuticke.
10. ŠKODA, J. Abhandlung über Perkussion und Auskultation. Wien, 1842. Braumüller and Seidel.
11. STERNBERG, M. Pericarditis epistenocardica. *Wein. med. Wschnschr.*, 1910.
12. SZULTRÉLY, G. and TOMORY, E. Beiträge zur Entstehung des präsystolischen (aurikulären) Geräusches. *Ztschr. f. Kreislaufforsch.*, 46: 179, 1957.

Early Transient Mid-diastolic Murmur in Rheumatic Fever*

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The development of cardiac murmurs during the course of rheumatic fever presents a most interesting problem. The pathogenesis and the role of the different parts of the heart in the production of the murmur are still not entirely clear.

We have become interested in the early appearance of an early diastolic or mid-diastolic murmur, which is not the result of mitral stenosis. Similar murmurs can be heard in patients with severe anemia, thyrotoxicosis or congestive failure. This survey is part of a more comprehensive investigation, which is being carried out in our department, concerning the course and development of the clinical signs of rheumatic fever.

From daily observations of children suffering from their first attack of rheumatic fever, we found that, in a considerable proportion of them, a mid-diastolic murmur appears as early as the first few days or the first two weeks after onset of the disease. Repeated auscultation has shown that this murmur is audible for a few days, sometimes up to a few weeks, and then disappears.

The appearance of the murmur coincides with the active stage of the disease; the disappearance of the murmur generally coincides with the improvement of the child's condition, when all the acute manifestations subside, both from a clinical and laboratory standpoint.

Recognition of the nature of this murmur is of importance for differential diagnosis, and is especially useful in preventing diagnostic and prognostic errors due to confusion with an already established mitral stenosis. This has been known for many years and has been described by various observers.[1–3]

More recently, Luisada et al.[4,5] and Zilli and Gamna[6] studied these murmurs by means of phonocardiograms, and proved the real nature of the murmur. However, the articles dealing with this subject describe the disappearance of the murmur over a period of months or years while, in our investigation, the murmur disappeared in the course of a few days or weeks. Therefore, we regard it as worthwhile to present this problem, illustrated by phonocardiographic documents.

Material and Method

The cases presented herein were selected from a group of patients with rheumatic fever who were hospitalized in our ward during the last two years. Of seventy-five patients, there was an early appearance of a medium-pitched mid-diastolic rumble in fourteen (18.5 per cent). In twelve of these fourteen children, this was the first attack of rheumatic fever. The ages ranged from three and a half to twelve years. There were eight males and six females. Three typical case histories are presented.

The tracings were recorded by means of a "Mingograf" Elema. This is a direct-writing, two-channel cardiograph with a phono amplifier and a frequency band selector from 1 to 6.

We used bands 4 and 5, which correspond respectively to 100 cps. (50 to 200 cps.) and 200 cps (100 to 400 cps.).

Case Histories

Case 1. M. Ch. was an eleven year old boy, whose illness started two weeks prior to admission, with a temperature of 39°C., and pains in the knees and ankles. A grade 4 systolic murmur was present over the apex and 2 cm. to its right. There were no thrills; the heart was normal in size on percussion. The lungs were normal, the liver and spleen were not palpable.

The erythrocyte sedimentation rate was 76 and 97 mm. per hour. The antistreptolysin titer was 2,500 units; white blood cells 7,600 per cu. mm. The electrocardiogram was normal and the phonocardiogram showed a systolic murmur. On x-ray examination, the cardiac shadow was normal.

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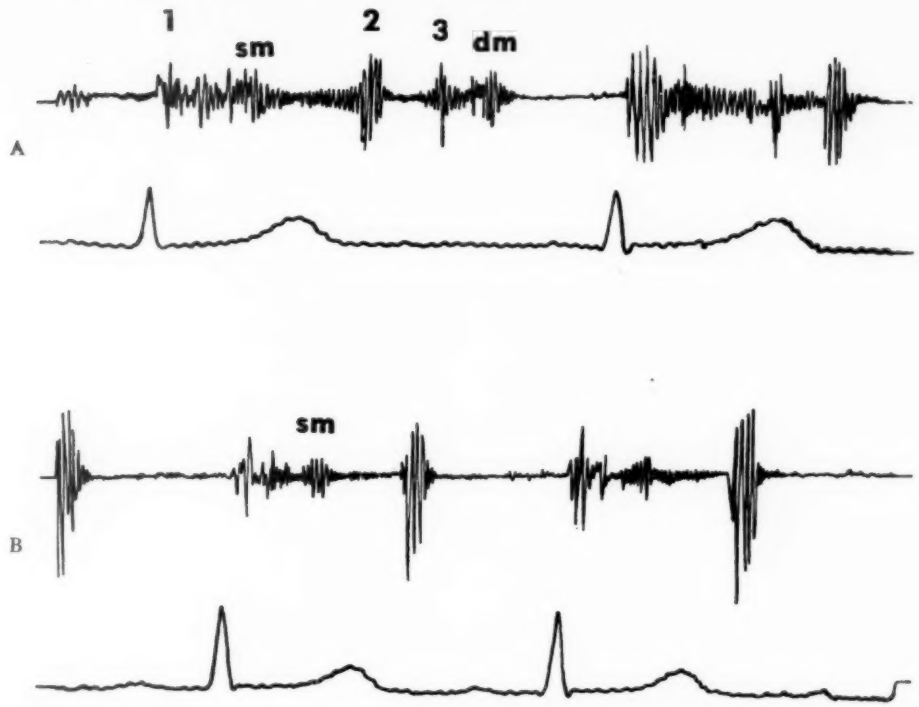

FIG. 1. Case 1. A, a systolic murmur (sm.) and a mid-diastolic rumble (dm.) beginning after the third heart sound. B, seventeen days later, following clinical improvement, the mid-diastolic rumble has disappeared. Only a low grade systolic murmur is present. (For purposes of clarity, free-hand artist's reproductions are shown instead of the original tracings.)

The patient was treated daily with 300 mg. of cortisone plus 6 gm. of salicylates. A grade 3 diastolic murmur appeared on the eighth day of hospitalization. The electrocardiogram then showed a marked depression of the ST segments. A phonocardiogram, recorded on the same day, showed systolic and mid-diastolic murmurs (Fig. 1A).

Following treatment, there was marked improvement; the temperature dropped to normal, the sedimentation rate decreased and the antistreptolysin titer became lower. On the twenty-ninth day of hospitalization, the temperature was normal; erythrocyte sedimentation rate 7 and 12 mm. per hour; antistreptolysin titer, 400 units. The electrocardiogram was improved. A phonocardiogram failed to show the diastolic murmur (Fig. 1B).

The child was discharged on the fortieth day in good general condition, with a normal electrocardiogram and chest x-ray, and only a low grade systolic murmur still present at the apex.

CASE 2. A. Y., a three and a half year old boy, was physically retarded; he had had repeated infections of the upper respiratory tract and tonsillitis. The patient became ill five days prior to admission with a temperature of 40°C. and an acute tonsillitis. The temperature dropped after three days of treatment with penicillin, but rose again two days later, accompanied by pain and swelling of the wrists and pain in the neck.

This undernourished child still had tonsillitis and enlarged cervical lymph nodes. The temperature was 39°C., the pulse rate 140 per minute. A loud blowing systolic murmur was noted at the apex. There was no thrill and no other cardiovascular finding. The lungs were normal; liver and spleen were not palpable.

The erythrocyte sedimentation rate was 135 and 145 mm. per hour; antistreptolysin titer, 400 units; white blood cells 16,000 per cu. mm.; the urine contained traces of albumin. The electrocardiogram was normal. X-ray examination of lungs and heart was within normal limits. Phonocardiogram showed a systolic murmur during the first half of systole; no diastolic murmur.

Penicillin therapy was instituted because of tonsillitis. Cortisone, 200 mg., and salicylates, 4 gm. a day, were started after the fever dropped on the sixth day of hospitalization. On the tenth day, the erythrocyte sedimentation rate was 136 mm. per hour, the antistreptolysin titer, 400 units. The liver was palpable 3 cm. below the costal margin. *A mid-diastolic, as well as a grade 4 systolic murmur, was heard and recorded* (Fig. 2A). The cortisone was replaced by Meticorten® (20 mg. per day) because of edema and moonface. There was an improvement

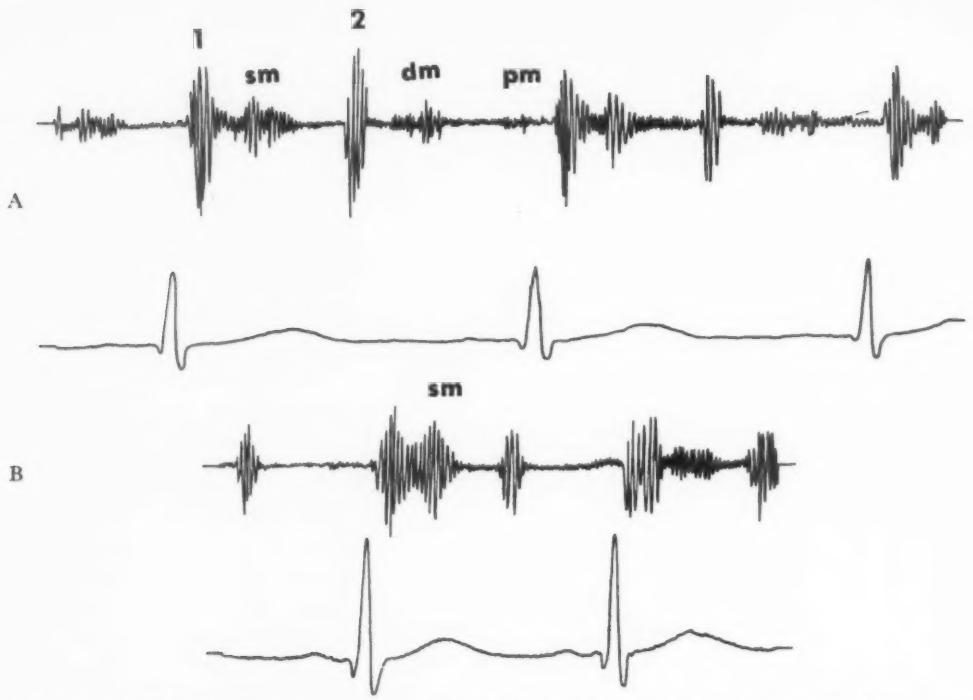

FIG. 2. Case 2. A, a systolic murmur (sm.), a mid-diastolic rumble (dm.) and a small presystolic murmur (pm.) are present. B, seventeen days later, following clinical improvement, the mid-diastolic rumble has disappeared while the systolic murmur is still present. (Artist's reproductions of original tracings.)

in his condition on the twenty-eighth day of hospitalization; the sedimentation rate dropped to 30 mm. per hour, the antistreptolysin titer to 133 units. The edema disappeared.

There was a mild rebound with decrease in Meticorten dosage but all signs disappeared after ten days without changing therapy. The diastolic murmur disappeared (Fig. 2B).

CASE 3. M. I., a seven year old, became ill four days prior to admission. The details are similar to those of the previous two cases. A significant feature was the roentgenographic outline of his heart during the disease because there was cardiac enlargement during the phase of the diastolic murmur, which subsided with the disappearance of the murmur.

COMMENTS

In all cases in which these murmurs were noted, they were located at the apex and midprecordium. There was *no* transmission to the left axilla and no thrill. There was *no* opening snap of the mitral valve but often a grade 3 to 4, medium-pitched third sound, was heard. On auscultation, the murmur was slightly harsh.

Bland et al.[1,2] suggested that the diastolic murmur in these cases might be caused by either relative stenosis of the orifice in relation to the dilated ventricular chamber of by vibrations set up by the diastolic filling of a dilated chamber with relaxed and atonic walls. Luisada et al.,[4,5] reviewing the problem with the aid of phonocardiographic tracings and analyzing the graphic differentiation of organic mitral stenosis from the so-called "relative" mitral stenosis, came to a similar conclusion.

A different concept had been advocated by Taquini et al.[3] "The audible extra sound appears in the phonocardiograms as a series of vibration which occur at the moment when the left ventricle is distended by rapid inflow, and is therefore a real third sound. In some cases prolongation of the vibration of the third sound may produce the acoustic effect of a rumble. In other cases, the vibration of the atrial sounds which occur very shortly after are superimposed upon the third sound and enhance the acoustic effect of a rumble." In other words, Taquini explained the murmur as a prolonged, amplified third sound.

After analyzing our cases and comparing the tracings with normal and abnormal tracings, in which third and fourth heart sounds were pres-

ent, we are of the opinion that *the diastolic murmur cannot be identified with the third or fourth heart sound, or with their prolongation. It cannot be confused with a real diastolic rumble of mitral stenosis because there is no mitral snap and because the murmur is often initiated by a large third heart sound, a fact which is rare in organic mitral stenosis.* In addition, comparison of the auscultatory findings with the x-ray and electrocardiographic findings supports the viewpoint of Bland et al. that the acute rheumatic process causes myocarditis and dilatation of the left ventricle, thus causing a "relative mitral stenosis." The normal streamlined flow through the mitral orifice is replaced by a turbulent flow, creating eddies within the ventricle.

Moreover, in the majority of cases, mitral regurgitation appears early, causing an increase in the quantity of blood of the left atrium and, therefore, an increase of the flow returning to the ventricle which will accentuate the acoustic effect.

Summary

An apical diastolic rumble often appears during the first episode of active rheumatic fever within the first week of the illness. It is associated with an abnormal apical systolic murmur due to mitral regurgitation.

Since mitral stenosis takes months or years to develop, such a diastolic murmur should not be regarded as being due to mitral stenosis.

Various theories were advanced about the origin of the murmur. We have explained it as being due to dilatation of the left ventricle.

The disappearance of the murmur within a few weeks coincides with the improvement of the patient's condition, and with the disappearance of the other clinical and laboratory signs of rheumatic activity.

The phonocardiographic tracings of two cases demonstrate the mid-diastolic murmur, which appeared early in the disease and subsequently disappeared.

References

1. Bland, E. F., White, P. D. and Jones, T. D. The development of mitral stenosis in young people with a discussion of the frequent misinterpretation of mid-diastolic murmur at the cardiac apex. *Am. Heart J.*, 9: 995, 1935.
2. Bland, E. F., Jones, T. D. and White, P. D. Disappearance of the physical signs of rheumatic heart disease. *J. A. M. A.*, 107: 569, 1936.
3. Taquini, C., Massell, B. F. and Walsh, B. J. Phonocardiographic studies of early rheumatic mitral disease. *Am. Heart J.*, 20: 225, 1940.
4. Luisada, A. A. and Perez Montés, L. A phonocardiographic study of apical diastolic murmurs simulating those of mitral stenosis. *Ann. Int. Med.*, 33: 56, 1950.
5. Luisada, A. A., Haring, O. M., and Zilli, A. B. Apical diastolic murmurs simulating mitral stenosis; graphic differentiation. *Ann. Int. Med.*, 42: 644, 1955.
6. Zilli, A. B. and Gamna, G. Evolution of murmurs in early rheumatic heart disease. *Am. J. Med.*, 17· 775. 1954

Murmurs Erroneously Attributed to Congenital Intracardiac Shunts*

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IT IS well known that children and adolescents may present systolic murmurs without any obvious congenital or rheumatic heart disease. Unfortunately, the clinical and graphic criteria for the differentiation of these murmurs from those caused by organic lesions of the heart and great vessels are still far from being exact. In many cases the decision that the murmur is an "innocent" one merely represents an act of faith, based on either psychologic elements or the personal experience of the observer.[1] Moreover, the fact that no evolution of heart disease can be foreseen still does not exclude discrete lesions of the heart valves, caused by bacterial or allergic mechanisms[1] or minimal congenital lesions.

Among the criteria which are usually accepted for diagnosis of an innocent murmur are: (1) location in the second and third left interspaces; (2) musical quality (groaning, crunching, dove-coo murmur; Still's murmur); and (3) short duration and clear-cut separation from both the first and second sound, best recognized by phonocardiography.[5]

Other criteria are: normal loudness of the heart sounds; no permanent splitting of the second sound; and possible changes in the characteristics of the murmur if the patient is repeatedly observed within a time span of several years.

The following cases are presented because: (1) the children presented murmurs and other cardiac abnormalities which led to the diagnosis of heart disease; (2) they were followed up in the Pediatric Cardiology Clinic or by private physicians for several years; and (3) right heart catheterization failed to disclose any shunt or severe valvular stenosis.

CLINICAL CASES

CASE 1. C. J., a fourteen year old Negro girl, was followed up in the Pediatric Cardiac Clinic for four years.

Past history included rheumatic fever at the age of two, with the development of migratory joint aches with swelling and redness, present intermittently for six months. She had had measles, chickenpox and whooping cough in early childhood, and frequent infections of the upper respiratory tract.

At the age of ten, the patient was seen in the Clinic because of chest pain, dyspnea, non-productive cough and generalized joint aches. She was then hospitalized and the diagnosis of sickle cell anemia was made.

On physical examination the heart was not enlarged on percussion; there was a grade 2 systolic murmur over the pulmonic area and apex. P_2 was louder than A_2 and constantly split.

The clinical impression was that of sickle cell anemia, possible rheumatic heart disease and possible atrial septal defect.

Blood tests indicated sickle cell anemia. An x-ray film of the chest showed no abnormal findings. Electrocardiographic studies showed evidence of right ventricular hypertrophy (Table I). A precordial phonocardiogram confirmed the auscultatory findings; there were no intracardiac murmurs (Table II, Fig. 1A). Cardiac catheterization was normal, with no shunts or valvular stenosis (Table III).

CASE 2. C. J., an eighteen year old Negro girl, was followed up in the Pediatric Cardiac Clinic for eight years because of a heart murmur, noted first at the age of six.

There was no definite history of rheumatic fever. The patient had had frequent infections of the upper respiratory tract, and an episode of joint pains and swelling at the age of six, accompanied by fever, lasting for about six days.

Physical examination showed that the heart was slightly enlarged to the left on percussion; the apical impulse was felt in the fifth intercostal space at the mid-clavicular line; a grade 3 apical and pulmonic systolic murmur was present. P_2 was louder than A_2 and widely split.

The clinical impression was that of rheumatic heart disease or atrial septal defect.

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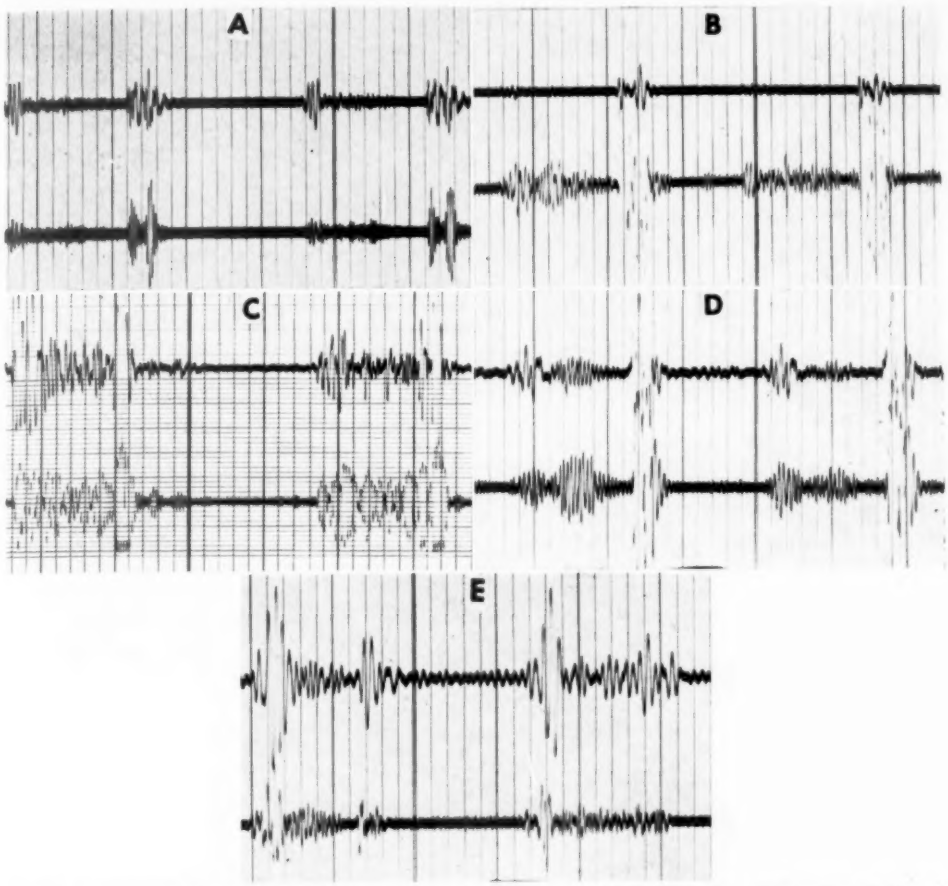

FIG. 1. Precordial phonocardiograms over pulmonic area of five patients. The upper tracing is a "stethoscopic" tracing, the lower tracing is a selective tracing (see ref. 3) recorded through a band pass filter in the band indicated below. A, Case 1. (150–250); faint systolic murmurs; widely split second sound. B, Case 2. (150–250); diamond-shaped systolic murmurs; large and split second sound; a few diastolic vibrations. C, Case 3. (150–250); all-systolic murmur (in the second cycle it has a crescendo phase in late systole); few early diastolic vibrations. D, Case 4. (120–240); diamond-shaped systolic murmur ending before the second sound; prolonged and large second sound. E, Case 6. (30–60); diamond-shaped systolic murmur ending before the second sound; split second sound.

TABLE I
Electrocardiograms

Case	Axis	Evidence of Ventricular Hypertrophy in Limb Leads	PR Interval (sec.)	QRS Duration (sec.)	V Leads
1. C. J.	Normal	Right	0.16	0.07	Inverted T waves in leads V_1R, V_1, V_2, V_3
2. C. J.	Normal	...	0.16	0.07	Evidence of right ventricular hypertrophy
3. D. D.	Normal	Left	0.13	0.18	Normal
4. G. C.	Normal	...	0.16	0.07	Normal
5. L. M.	Right	Right	0.14	0.07	T waves inverted in leads V_3R, V_4R, V_1, V_2
6. L. B.	Normal	...	0.12	0.08	Normal
7. R. R.	Right	Right	0.13	0.08	Tall R waves in leads V_4R and V_3R Inverted T waves in leads V_4R, V_3R and V_1
8. S. F.	Left	...	0.12	0.08	Tall T waves in leads V_2, V_3 and V_4

TABLE II
Precordial and Intracardiac Phonocardiograms

Case	Precordial Phonocardiogram	Intracardiac Phonocardiogram (Right Heart)
1. C. J.	Small, early systolic murmur over the entire precordium, loudest at pulmonic area; widely split P_2 with delayed and prolonged pulmonic component	No murmurs
2. C. J.	Prolonged systolic murmur at pulmonic area; third heart sound at apex; constantly split P_2	.....
3. D. D.	All-systolic murmur over entire precordium, loudest at apex and fifth intercostal space; early diastolic rumble at apex and pulmonic area; loud, prolonged second pulmonic sound	.....
4. G. C.	Diamond-shaped, systolic, rather musical murmur over pulmonic area; systolic and diastolic murmurs over mid-precordium; prolonged, loud and occasionally split P_2	Moderate systolic murmur in pulmonic area; minimal systolic murmur in right atrium
5. L. M.	Diamond-shaped systolic murmur of moderate amplitude over pulmonic and aortic areas; constantly split P_2	Short systolic murmur in pulmonic area; a few systolic vibrations in right ventricle
6. L. B.	Large and prolonged diamond-shaped systolic murmur over entire precordium; constant splitting of P_2	Large, diamond-shaped systolic murmur in pulmonic area
7. R. R.	Minimal systolic murmur recorded; constantly split P_2	No murmurs; large third sound in pulmonic area; large fourth sound inferior vena cava and right atrium
8. S. F.	Prolonged systolic murmur at the apex; diamond-shaped systolic murmur over pulmonic and aortic areas; constantly split P_2	.....

TABLE III
Right Heart Catheterization Data (mm. Hg.)

Case	Right Atrium (mean)	"Wedge" Pressure	Right Ventricle (S/D)	Main Pulmonary Artery (S/D/M)	Diagnosis from Pressure and Oximetry Readings
1. C. J.	4.7	8.2	26/2–5.5	25/8/10	No shunts, no stenosis
2. C. J.	4.0	9.0	20.2/1.9	18.1/12/6.8	No shunts, no stenosis
3. D. D.	3.0	..	28/2.4	28/8/14	No shunts, no stenosis
4. G. C.	0.6	7.5	18.5/0.4–3	17/6.5/11.2	No shunts, no stenosis
5. L. M.	4.4	7.0	23/2–4	23/9/11	No shunts, no stenosis
6. L. B.	3.8	8.1	37.5/6.2	33.5/6.7/16.9	No shunts (no significant stenosis)
7. R. R.	0–4	..	20/0–4	22/10/15	No shunts, no stenosis
8. S. F.	4.0	12.5	28/0.3	24/10/16	No shunts (no significant stenosis)

An x-ray film of the chest showed that the heart was enlarged to both left and right, the pulmonary artery was prominent and pulmonary vascular markings were increased (Fig. 2A). Electrocardiographic findings indicated right ventricular hypertrophy (Table I). Phonocardiograms showed a prolonged pulmonic systolic murmur and split P_2 (Table II, Fig. 1B). Cardiac catheterization was normal, with no shunts or stenosis (Table III).

CASE 3. D. D., a six year old Negro girl, was first seen at the hospital because of an episode of cough, elevated temperature, dyspnea and vomiting.

Past history included a heart murmur first heard at the age of two and a half when she was treated for a "cold." The child did not walk until two years of age. She had had scarlet fever at five. Her history was negative for rheumatic fever; she had recurrent sore throats.

Physical examination showed that the patient was in respiratory distress. Pulse was 140 and regular; blood pressure, 102/60 mm. Hg.; temperature, 103° F.; respiration, 30/minute. Dullness and crepitant rales were heard over the apex of the left lung; the heart was enlarged with boot configuration on percussion. There was a grade 4 rough systolic murmur over the entire precordium, loudest at the apex. A

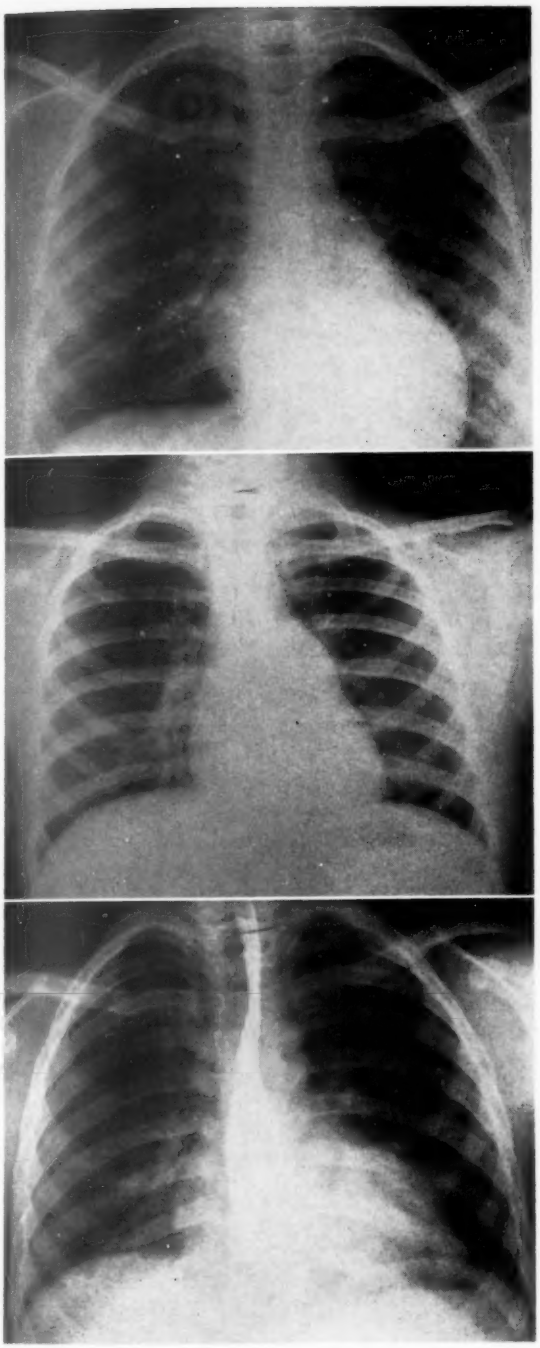

FIG. 2. Chest films. *Top*, Case 2. *Middle*, Case 3. *Bottom*, Case 7.

questionable mid-diastolic murmur was present at the apex; P_2 was very loud and split. The abdomen was negative for abnormalities; the extremities were poorly developed.

The patient was given penicillin and digitalis, with prompt response and improvement. A few weeks later she was readmitted to the hospital because of dyspnea, elevated temperature and chest pain. The physical findings were essentially the same, but there was no response to treatment which included the administration of oxygen, digitalis, Mercuhydrin® and antibiotics. The patient died the same day.

The clinical impression was that of Marfan's syndrome and congenital heart disease (possible rheumatic heart disease).

An x-ray film of the chest showed an enlarged right ventricle and a relatively small vascular pedicle. Vessels of the right lung were increased. There was a possibility of a ventricular or atrial septal defect (Fig. 2B).

Electrocardiographic findings indicated left ventricular hypertrophy (Table I).

Phonocardiograms showed systolic and diastolic murmurs (Table II, Fig. 1C). On cardiac catheterization, the right ventricular pressure was slightly elevated; no shunt or stenosis was noted (Table III).

The pathologic diagnosis was Marfan's syndrome with endocardial fibroelastosis predominant in the left heart; no shunts; mitral stenosis and insufficiency.

CASE 4. G. C., a nine year old Negro girl, had been followed up at the Pediatric Cardiac Clinic for three years since the age of six when a heart murmur was noted.

Her history was negative for rheumatic fever. She had had measles at the age of four, and frequent infections of the upper respiratory tract during infancy.

On physical examination the following were noted: no thrills; an apical impulse in the fifth intercostal space at the mid-clavicular line; a harsh grade 3 systolic murmur at the pulmonic area and mid-precordium; P_2 was louder than A_2 and constantly split. The liver was palpated two fingerbreadths below the costal margin.

The impression was that of an atrial septal defect.

An x-ray film of the chest was normal (following barium swallow). Central and peripheral pulmonary vascular markings were not increased. The electrocardiogram was normal (Table I). Moderate systolic and diastolic murmurs were noted on the external phonocardiogram, and a systolic murmur on the intracardiac phonocardiogram (Table II, Fig. 1D). Cardiac catheterization was normal (Table III).

CASE 5. L. M., a six year old Negro boy, had been followed up at the Pediatric Cardiac Clinic for four years since the age of two because of a heart murmur.

His history was negative for rheumatic fever. He had had frequent episodes of epistaxis (three to four each month) since the age of four; he also had measles at that age.

On physical examination a grade 1-2 apical systolic murmur was noted; there was a grade 2 systolic

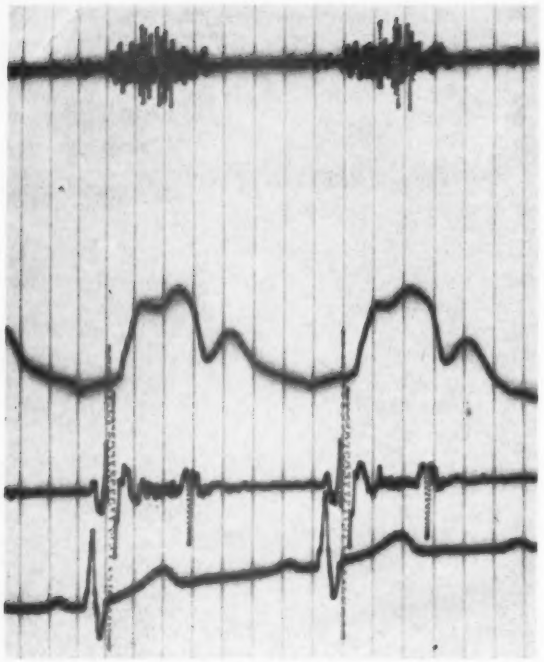

FIG. 3. Intracardiac phonocardiogram (upper record) and pressure tracing (second from above) of the pulmonary artery in Case 6. Diamond-shaped systolic murmur.

murmur at the pulmonic area. P_2 was louder than A_2 and constantly split.

The impression was that of an atrial septal defect.

An x-ray film of the chest showed a prominent left hilus and normal peripheral pulmonary vascular markings. The electrocardiogram indicated right ventricular hypertrophy (Table I). A moderate pulmonic systolic murmur was noted in the external and intracardiac phonocardiograms (Table II). Cardiac catheterization was normal (Table III).

CASE 6. L. B., a nine year old white boy, had been followed up at the Pediatric Cardiac Clinic for three years since the age of six when a heart murmur was noted on a routine check-up.

His history was negative for rheumatic fever. He had had episodes of bronchial asthma at four to five years, tonsillectomy at five and measles and chickenpox at four.

On physical examination there was a systolic murmur, grade 2–3, over the left sternal border from the second to the fourth intercostal space; P_2 was split.

The impression was that of an atrial septal defect.

An x-ray film of the chest showed left ventricular enlargement; pulmonary vascular markings were within normal limits. The electrocardiogram was normal (Table I). A loud diamond-shaped systolic murmur was noted in the precordial and intracardiac phonocardiograms (Table II, Figs. 1E and 3). Cardiac catheterization showed a slightly elevated right ventricular pressure; the pulmonic valve gradient was minimal (Table III).

CASE 7. R. R., a ten year old white girl, had been followed up by a private physician because of a heart murmur noted in early infancy. The patient was always asymptomatic.

Her history was negative for rheumatic fever. She had had two episodes of pneumonia at the age of nine and several attacks of bronchial asthma since that age.

Physical examination was essentially within normal limits with the exception of a faint systolic murmur at the apex and a grade 2 soft systolic murmur at the pulmonic area; P_2 was inconstantly split.

The impression was that of a possible atrial septal defect.

The pulmonary artery was dilated in the first x-ray film taken in 1956. This became more and more accentuated in the recent films. The bronchovascular markings were normal and so were the hilar shadows (Fig. 2C).

Electrocardiography indicated right ventricular hypertrophy (Table I). The phonocardiogram showed a minimal systolic murmur, with loud third and fourth sounds in the intracardiac phonocardiogram (Table II). Cardiac catheterization was normal (Table III).

CASE 8. S. F., an eleven year old white girl, had been followed up in the Pediatric Cardiac Clinic for four years because of a heart murmur since early infancy.

Her history was negative for rheumatic fever; she had had measles and mumps.

On physical examination a grade 3 soft systolic murmur was heard over the mid-precordium, a grade 2–3 systolic murmur over the pulmonic area; $P_2 < A_2$.

The impression was that of pulmonary stenosis.

An x-ray film of the chest showed an elongated heart and an enlarged right atrium; bronchovascular markings were not increased. The electrocardiogram was normal (Table I). The phonocardiogram showed an apical and pulmonic systolic murmur (Table II). Cardiac catheterization indicated right ventricular pressure slightly elevated(?); no shunt or stenosis; wedge pressure slightly elevated (Table III).

COMMENTS

AUSCULTATION—PHONOCARDIOGRAPHY

The systolic murmur observed in these children did not conform to the criteria usually employed for recognition of an "innocent" murmur.

Location: In Cases 3 and 8 it was maximal at the apex; in Case 5 it was equally audible at the second right and at the second left interspaces; in Case 4 it was equally audible over all precordial areas.

Pitch: The murmur had a "musical" or

"groaning" quality only in one case (Case 4) of eight.

Phase: The murmur was separated from the second sound only in Cases 1 and 6 (two of eight); in none was it separated from the first sound.

Loudness: The murmur was grade 3 to 4 in half the cases. In Case 7, in which there was only a grade 1 murmur, attention was called to the heart by the remarkable dilatation of the pulmonary artery (Fig. 2C).

Abnormalities of the heart sounds: The second sound was constantly split over the pulmonic area in six of eight cases.

Diastolic murmur: A diastolic murmur was heard and recorded in two of eight cases.

ELECTROCARDIOGRAM

Evidence of right ventricular hypertrophy was found in four cases; left ventricular hypertrophy was noted in one. Thus, five of eight patients had an abnormal electrocardiogram.

CHEST X-RAY

Five of eight patients had abnormal findings. These consisted of right ventricular enlargement in Case 3; right atrial enlargement in Case 8; both right and left ventricular enlargement in Case 2; left ventricular enlargement in Case 6; pulmonary artery dilatation in Cases 2 and 7; and increased vascular markings in Case 2.

RIGHT HEART CATHETERIZATION

No evidence of left-to-right shunt was found in any of the cases. The right atrial pressures were normal. The right ventricular pressures were slightly elevated in Cases 3, 6 and 8. In Cases 6 and 8 there was a minimal gradient of 4 mm. Hg. across the pulmonic valve. It is interesting to note that the patient presenting the largest pulmonary artery (Case 7) had no gradient across this valve.

The pulmonary "wedge" pressure was normal in all patients except one (Case 8), in whom it was slightly above normal. It is unfortunate that this determination had not been made in Case 3, in which autopsy disclosed fibroelastosis of the left heart.

EXTERNAL PHONOCARDIOGRAPHY

Phonocardiograms were recorded in all cases with the technic of "selective phonocardiography."[3] The typical patterns of the murmurs were consistently recorded for several years (Fig. 1).

INTRACARDIAC PHONOCARDIOGRAPHY

An intracardiac phonocardiogram was recorded in five of the eight cases, those chronologically studied after 1957, according to the method of Luisada and Liu.[2] This method, in contrast with those based on the use of an intracardiac microphone, does *not* show any systolic vibration in normal subjects.

In two patients (Cases 1 and 7) no murmur was demonstrated in the chambers of the right heart or in the pulmonary artery. On the other hand, murmurs were demonstrated in Cases 4, 5 and 6. A moderate systolic murmur was recorded in the two former cases, particularly in the pulmonary artery, while an extremely large, diamond-shaped systolic murmur was recorded in this vessel in Case 6 (Fig. 3).

Thus, intracardiac phonocardiography proved of value in the identification of the chamber or vessel in which the murmur was produced. This is consistent with the observations of Luisada and Liu[4] in patients with a rheumatic mitral valve: the murmur of mitral insufficiency was recorded in cases in which the pattern of left atrial pressure was nearly normal, indicating the greater sensitivity of intracardiac sound tracings in comparison with pressure tracings. It is interesting to note that while the most dilated pulmonary artery (Case 7) was not associated with any intravascular murmur, the patient with the loudest intravascular murmur (Case 6) had a slightly elevated right ventricular pressure and a minimal gradient across the pulmonic valve. Whether there was a relationship of cause and effect is difficult to say, but it is possible.

In the evaluation of the various data it should be kept in mind that only the right heart was explored in the patients under study. The clinical picture was not considered of such severity as to warrant exploration of the left heart. It is possible that the latter, if performed, would have permitted identification of the cause of the murmurs in those cases in which no murmur was found in the right heart.

Conclusions

In eight clinical patients, followed up for several years, loud murmurs and a split second sound, or electrocardiographic and roentgenologic abnormalities, led to the erroneous diagnosis of a congenital intracardiac shunt. Right heart catheterization failed to disclose any shunt but revealed a minimal pulmonic gradient in two cases, a slight increase of right ventricular

pressure in three, and a slight increase of the pulmonary wedge pressure in one. Intracardiac phonocardiography, performed in five cases, revealed small pulmonic (and right ventricular) murmurs in two and a large pulmonic murmur in one.

A final interpretation of the cause of the murmurs and other abnormalities was possible only in a few cases, as follows: Case 1, anemia; Case 3, fibroelastosis, lesions of the mitral valve (autopsy); Case 4 and 5, probable pulmonic systolic murmur, cause unknown; Case 6, pulmonic systolic murmur, possibly due to minimal pulmonic stenosis; Case 7, dilatation of pulmonary artery due to repeated episodes of bronchial asthma (possibly favored by arteritis or congenital weakness of the vessel); Case 8, possible lesion of the mitral valve.

Summary

Eight clinical patients, followed up for several years and presenting loud murmurs or other auscultatory, electrocardiographic or roentgenologic abnormalities, were erroneously diagnosed as having congenital intracardiac shunts. Subsequent studies, including right heart catheterization in all, intracardiac phonocardiography in five, and autopsy in one, failed to disclose congenital shunts. Fibroelastosis of the left heart existed in one. Tentative, although not completely proved diagnoses, are presented for some of the others.

References

1. Luisada, A. A., Haring, O. M., Aravanis, C., Cardi, L., Jona, E. and Zilli, A. B. Murmurs in children. A clinical and graphic study in 500 children of school age. *Ann. Int. Med.*, 48: 597, 1958.
2. Luisada, A. A. and Liu, C. K. Simple methods for recording intracardiac electrocardiograms and phonocardiograms during left or right heart catheterization. *Am. Heart J.*, 54: 531, 1957.
3. Luisada, A. A., Richmond, L. and Aravanis, C. Selective phonocardiography. *Am. Heart J.*, 51: 221, 1956.
4. Luisada, A. A. and Liu, C. K. Intracardiac phonocardiography in mitral and aortic valve lesions. *Am. J. Cardiol.*, 1: 379, 1958.
5. Wells, B.: The graphic configuration of innocent systolic murmurs. *Brit. Heart J.*, 19: 124, 1957.

Real and Apparent Apical Impulse in Tricuspid Lesions

Differentiation of Mitral and Tricuspid Murmurs and Sounds*

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In a paper published in 1946 on the diagnosis of tricuspid regurgitation[1] it was concluded that: (1) tricuspid systolic murmurs are reinforced during postinspiratory apnea while aortic and mitral systolic and diastolic murmurs decrease in intensity during this same phase, and (2) postexpiratory apnea increases aortic and mitral murmurs and decreases the intensity of the tricuspid murmurs.

In 1950, one of us[2] described several physical data which are useful for the diagnosis of tricuspid stenosis: increase during postinspiratory apnea of the diastolic and presystolic murmurs, of the opening snap of the tricuspid valve and of the first sound. In 1951–1952, other observations were published on the cardiac and peripheral phenomena associated with stenosis and regurgitation of the tricuspid valve.[3,4] In some patients, the tricuspid murmurs did not increase until after two or more inspirations and occasionally the murmurs decreased during inspiration. The senior author and Ramirez Jaime[4] later ascertained that the reason for this was the presence of a large, degenerated and translucent right atrium, which they named "atrium papiraceoum."

In 1951 the senior author and his co-workers[4] described the relative stenosis of the tricuspid valve in patients with chronic cor pulmonale due to pulmonary emphysema and mediastinal fibrosis[4] or idiopathic pulmonary hypertension, and in patients with rheumatic valvular disease without organic tricuspid lesions. In all these cases, there was a remarkable dilatation of the right cardiac chambers. They were further able to prove that the murmur audible at the apex was equally reinforced during postinspiratory apnea, a fact which led to the erroneous belief that some mitral murmurs acted as tricuspid murmurs. This fact was claimed to decrease the value of the previously described signs.

Certain hemodynamic principles are basic and operate both in physiologic conditions and in clinical cases. Therefore, it does not seem logical for mitral murmurs to increase during postinspiratory apnea. The analysis of this phenomenon and of its mechanism led to the conclusion that there must have been an error of interpretation. A possibility was the fact that the "apex" beat was actually the impulse of the enlarged right ventricle. If this were true, then *the murmurs heard in this area originated in the tricuspid valve and not in the mitral valve.*

Method and Material

With this hypothesis and the previous studies of patients with tricuspid lesions, we tried to ascertain the real site of the cardiac apex, i.e., that area which belongs to the left ventricle.

We proceeded to localize the apical beat in the left lateral position in patients with mitral and tricuspid lesions and we made different auscultations in several points of the left precordium. In some patients, at this particular site, postinspiratory apnea caused the murmurs and sounds to follow the general behavior of murmurs and sounds originating in the right cardiac chambers.[8–13] Significant differences were noted by listening in the area between the apparent apex and the anterior or posterior

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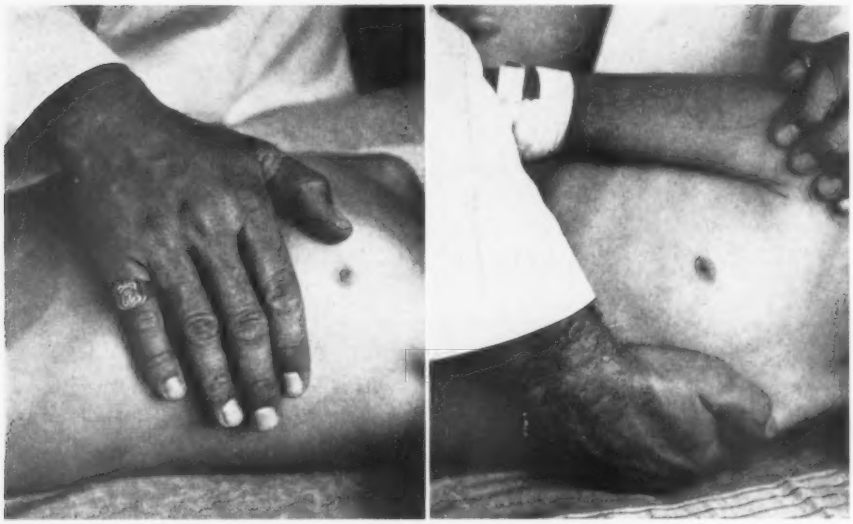

FIG. 1. Method for the identification of the "apparent apex" in the recumbent position (*left*); and the "real apex" in the left lateral position (*right*).

axillary lines. Actually, a new auscultatory area was found at the anterior axillary line which we called the "real apex," where murmurs and sounds differed in quality from those found at the "apparent apex" and decreased during postinspiratory apnea, thus following the typical hemodynamic behavior of the left cardiac chambers. This was, therefore, the *mitral area*. Once this fact was ascertained, we sought for a new apical impulse in different positions; it was discovered in the left lateral position (Pachon's method). This was the solution to our problem.

For statistical purposes, 200 patients with tricuspid lesions (a common complication in Mexico) were studied. In thirty of them, the diagnosis was confirmed at autopsy. In 12 per cent of the cases, the "true" and "apparent" apex phenomenon was present. All of them had advanced mitral and tricuspid lesions. The electrocardiogram, chest x-ray, phonocardiogram, apex cardiogram and autopsy records were studied.

Clinical Observations

DESCRIPTION OF THE SIGN AND HOW TO DISCOVER IT

When the apex beat is located in the recumbent position, the palm of the right hand is placed over this area; this apical beat is the "apparent" one; the tips of the fingers will then be reaching the axillary lines somewhere between the fourth and sixth left intercostal spaces. Without removing the right hand from this position, the patient is then made to turn to the left lateral recumbent position (Fig. 1). At this time a new apical impulse appears which was not previously apparent or was doubtful; this is caused by the "real" apex. It is felt from 6 to 12 cm. from the apparent apex, according to the age of the patient and the shape of the chest. The murmurs and sounds produced at the mitral valve are clearly heard in this area. The inspiratory and expiratory changes noticed in this apical region behave according to the hemodynamic changes of the left heart.

With the patient in the recumbent position, an increase of the intensity of the apical beat is generally felt; it is displaced minimally giving the impression that it never disappears, and this is even more clearly perceptible if a thrill is present. On the contrary, if there is a "real" and an "apparent" apex, a second apical beat appears under the tips of the fingers of the exploring hand.

ANATOMICAL DATA

Enlargement of the right cardiac chambers displaces the cardiac apex outwards and posteriorly. This fact is particularly noticeable in patients with old tricuspid lesions. The consequent clockwise rotation of the heart around the longitudinal axis and the counterclockwise rotation around the transverse axis causes a considerable backward displacement of the left ventricle. The right atrium and

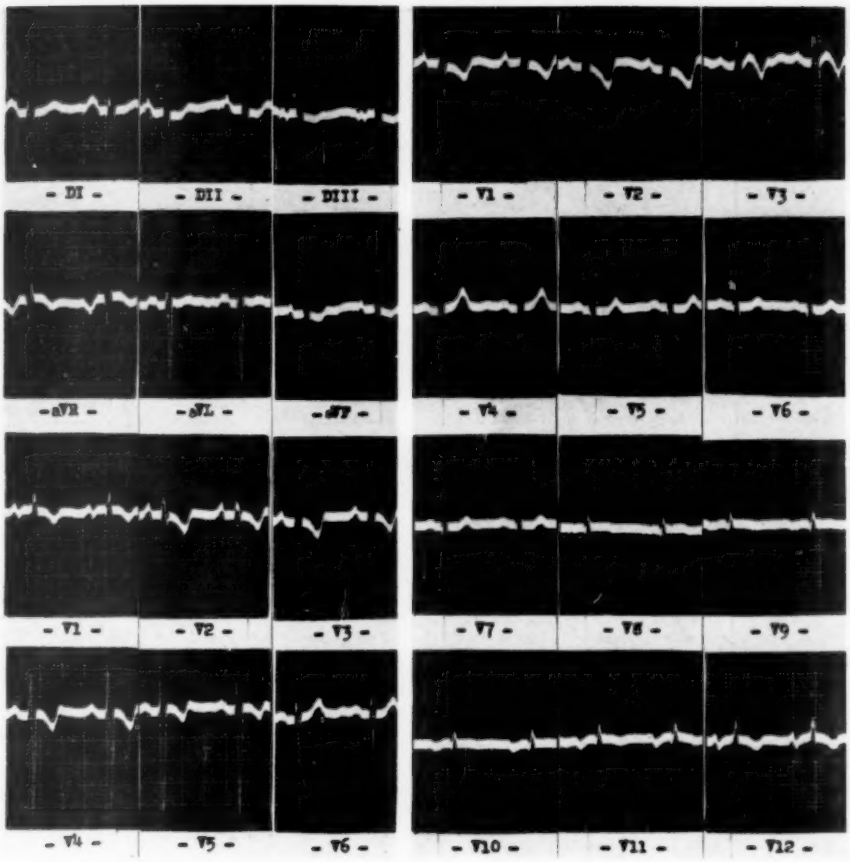

FIG. 2. *Left*, electrocardiogram of a patient with mitral and tricuspid lesions with marked right axis deviation. The patterns in leads V_1 to V_5 are those of the right ventricle; left ventricular patterns appear only in V_6. *Right*, circumferential chest leads recorded at the level of lead V_5; the transitional zone is displaced to the left (lead V_4). (Courtesy of Dr. Cisneros.)

ventricle then form the anterior aspect of the heart. Autopsies performed by Costero, Barroso, Chévez, Monroy and Contreras have proved this fact.

ELECTROCARDIOGRAPHIC FINDINGS

The electrocardiogram, through the pattern of the unipolar precordial leads, shows the area of the heart where the exploring electrode is placed.

Since the classic work of Wilson et al.,[14] it is accepted that leads V_1 and V_2 correspond to potential variations of the right ventricle; leads V_3 and V_4 to those of the ventricular septum (transitional zone); and leads V_5 and V_6 to those of the left ventricle. Ferrero et al.[15] have reached the same conclusions. A displacement of the transitional zone to the left indicates that the heart has rotated around its longitudinal axis in a clockwise direction.

Direct unipolar recordings made by Barbato[16] indicate that the right ventricle represents the greatest part of the anterior aspect of the heart in patients with mitral disease. Recent studies by Cisneros, Fishleder and Sodi-Pallares[17] on the electrocardiogram in rheumatic valvular disease further support this concept because right ventricular overload causes a marked clockwise rotation around the longitudinal axis and displacement of the transitional zone to the left.

In patients with "real" and "apparent" apex, the transitional zone is displaced to lead V_4 or further, and the left ventricular pattern starts at leads V_5 or V_6 (Fig. 2).

RADIOLOGIC FINDINGS

Dorbecker has given a demonstration of the site of the real apex (left ventricle) by means of fluoroscopy and with selective x-rays through

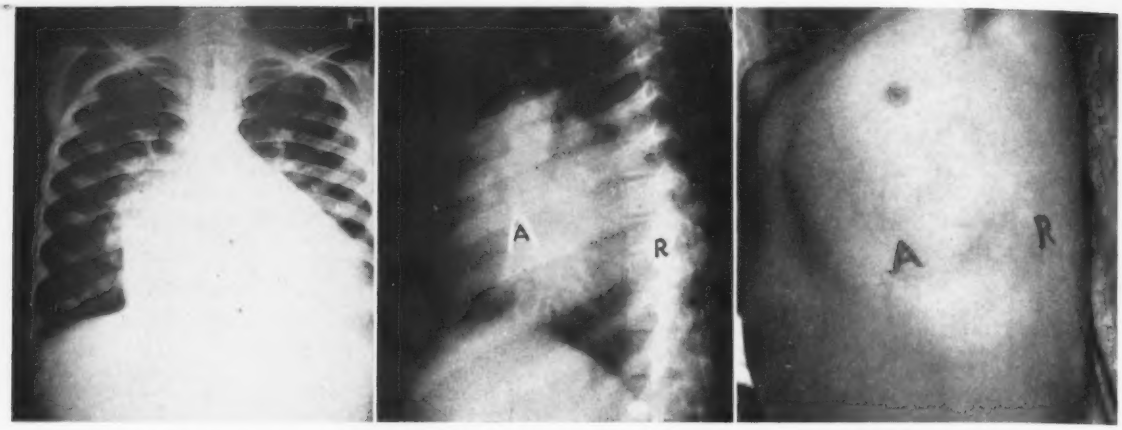

FIG. 3. *Left*, chest roentgenogram in the frontal view. The space of clear lung field between the chest wall and the heart is resonant to percussion, a fact which permits an accurate location of the apex. *Center*, left oblique view at 60 degrees. The letter *A* corresponds to the anterolateral aspect of the right ventricle and to the site found by palpation ("apparent" apex). The letter *R* is at the site of the "real" apex (left ventricle). These facts are confirmed fluoroscopically. *Right*, the chest of the same patient. The letter *A* corresponds to the "apparent" apex; the letter *R* to the "real" apex found clinically. (Courtesy of Drs. Dorbecker, Corominas and Ambia.)

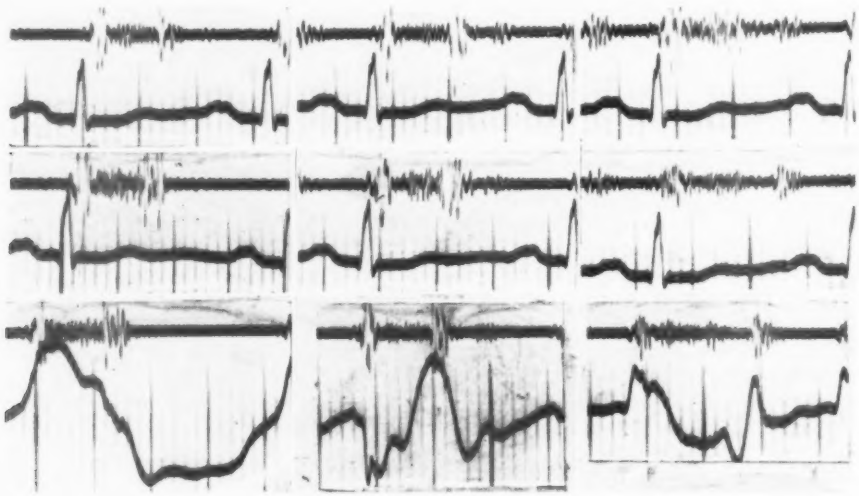

FIG. 4. Phonocardiograms and apex cardiograms. The tracings on the *left* are recorded over the xiphoid area; those in the *center*, over the "apparent" apex; those on the *right* over the "real" apex. *Top:* phonocardiograms during postexpiratory apnea; *Middle:* phonocardiograms during postinspiratory apnea; *Bottom:* low frequency apex tracings (cardiograms). Notice the reinforcement of tricuspid murmurs during postinspiratory apnea (*middle*) at the xiphoid and apparent apex, and their decrease at the real apex. In the upper records (*top*), taken during postexpiratory apnea, the murmurs decrease over the xiphoid and "apparent" apex areas (*left* and *center*) while they increase at the "real" apex (*right*). (Courtesy of Drs. Fishleder and Avila Cos.)

the use of markers. The site of the apex at fluoroscopy coincided with that found clinically (Fig. 3).

Cineangiocardiographic studies by Dorbecker show that, in these cases, the right ventricle occupies the anterior aspect of the heart including the area normally filled by the left ventricle.

Roentgenology has also proved that the heart, in the left lateral position, displaces the margins of the left lung, thus permitting the left ventricle to come in contact with the chest wall at one of the axillary lines.

PHONOCARDIOGRAPHIC FINDINGS

Fishleder[19] has given proof that murmurs and

sounds of the real apex originate in the mitral valve, since they decrease in postinspiratory apnea and increase in postexpiratory apnea. On the contrary, over the apparent apex, the murmurs and sounds originate in the tricuspid valve and increase during inspiration (Fig. 4). At times, extraneous acoustic phenomena originating in different valves invade these areas. Thus, a high-pitched mitral systolic murmur may appear during postexpiratory apnea in the tricuspid area. This phenomenon is at times seen in greatly dilated hearts with considerable rotation. In these cases, differentiation is made specially by comparing the auscultatory data in the phases of postinspiratory and postexpiratory apnea.[1–3]

The *apical cardiogram*, studied by Avila Cos[18] under the direction of Fishleder, also indicates the patterns of the right and left ventricular impulses. The cardiogram recorded at the xiphoid (tricuspid area) shows a large positive wave in systole (Fig. 4). On the contrary, the tracing obtained in the seventh left intercostal space at the mid-axillary line shows fundamentally a systolic depression with a small positive wave at the beginning of ejection. The cardiogram registered at the fifth left intercostal space and the mid-clavicular line shows a diphasic (minus-plus) wave during systole.

The cardiograms suggest that, during ejection, the heart oscillates clockwise around its longitudinal axis causing the right ventricle to move forward and the left ventricle backward. This is commonly seen in predominant right-sided enlargements. At the fifth left intercostal space and the mid-clavicular line, the precordial motions are influenced by both ventricles, although more so by the right. The presence of a positive wave at the beginning of ejection in the cardiogram at the seventh left intercostal space and the mid-axillary line suggests that, although right ventricular enlargement predominates, there is also a certain degree of left-sided enlargement.

The systolic murmur and the loud third sound, coinciding with a large third wave in the cardiogram, reveals the existence of significant mitral regurgitation associated with the stenosis of the mitral and tricuspid valves. (Fig. 4).

Comments

The morphologic changes occurring in the heart when greater or lesser dilatation of the right cardiac chambers occurs have been the subject of anatomic studies with or without postmortem filling of the chambers. These were confirmed by electrocardiographic and cineangiocardiographic studies *in vivo*. Pathologic, electrocardiographic, roentgenologic and clinical studies reveal that the right ventricle occupies the anterolateral aspect of the chest, while the left ventricle is pushed backwards. Electrocardiography reveals that these changes are due to clockwise rotation around the longitudinal axis and counterclockwise rotation around the transverse axis.

These rotations explain why there is an "apparent" apex beat due to impulse of the dilated right ventricle, which has come into close contact with the chest wall. The left ventricle, on the other hand, comes in contact with the chest wall near the anterior axillary line by displacing the margin of the lung.

In chronic cases of cor pulmonale previously studied,[5,6] these rotations were also present; there were systolic and diastolic murmurs at the tricuspid area, the latter being due to relative stenosis. In these patients, a "real" and an "apparent" apical impulse were also found. In some cases of congenital heart disease with right ventricular enlargement, the same phenomenon may be observed.

The test described permits clear differentiation between mitral and tricuspid phenomena at the correct corresponding areas, clinical evaluation of the enlargement of the right ventricle, and estimation of the rotation of the heart around its axis.

Summary and Conclusions

While studying patients with tricuspid lesions it was discovered that some showed a reinforcement of the murmurs during postinspiratory apnea at the mitral area (apparent apical impulse). This seemed to decrease the importance of signs which had been previously described by one of us (R. C.) for the diagnosis of tricuspid valve lesions.

The present study ascertained the following facts:

1. When there is right ventricular enlargement, the heart presents a clockwise rotation around its longitudinal axis and a counterclockwise rotation around its transverse axis; then, the left ventricle is displaced backwards while the right occupies the anterolateral aspects of the heart.

2. This extreme rotation is confirmed radiologically.

3. The electrocardiogram shows a right ventricular pattern over the anterior aspect of the heart and that of the left ventricle only from lead V_5 on.

4. The phonocardiogram shows that the acoustic phenomena corresponding to the mitral valve occur at the left axillary line ("real" apex) while those corresponding to the tricuspid valve are found over the area of the "apparent" apex.

5. The apical cardiogram records the pattern of the right ventricle over the "apparent" apex and that of the left ventricle over the "real" apex.

6. A method is described which permits the differentiation between the "real" apex and the "apparent" apex by careful palpation of the apical and adjacent areas in the left lateral decubitus.

7. Once the "real" and "apparent" apex are identified, the behavior of murmurs and sounds of the tricuspid valve is recognized as in other, more common, cases.

References

1. Rivero-Carvallo, J. M. Signo para el diagnóstico de las insuficiencias tricuspídeas. *Arch. Inst. cardiol. México*, 16: 231, 1946.
2. Rivero-Carvallo, J. M. El diagnóstico de la estenosis tricuspídea. *Arch. Inst. cardiol. México*, 20: 1, 1950.
3. Rivero-Carvallo, J. M. Semiologia de las lesiones tricuspídeas. *Arch. Inst. cardiol. México*, 21: 567, 1951; *Arch. mal. coeur*, 2: 1329, 1952.
4. Rivero-Carvallo, J. M., Carral, R. and Ramirez Jaime, M. H. Estenosis relativa de la tricuspide. *Arch. Inst. cardiol. México*, 21: 47, 1951.
5. Rivero-Carvallo, J. M. and Ramirez Jaime, M. H. El diagnóstico de la auricula papiracea. To be published.
6. Rivero-Carvallo, J. M., Carral, R. and Ramirez Jaime, M. H. El diagnóstico de la estenosis—relativa de la tricuspide. *Arch. Inst. cardiol. México*. To be published.
7. Rivero-Carvallo, J. M. and Perrin Chico, M. Las mediastinitis reumáticas. *Arch. Latino. am. de Cardiol. y hemat.*, 13: 171, 1943.
8. Cournand, H. Recent observations on the dynamics of the pulmonary circulation. *Bull. New York Acad. Med.*, 23: 51, 1947.
9. Lauson, H. D., Cournand, A. and Bloomfield, R. A. Influence of respiration on circulation in man, with special reference to pressures in the right auricle, right ventricle, femoral artery and peripheral veins. *Am. J. Med.*, 1: 315, 1946.
10. Cournand, A., Riley, R. L., Bredd, E. S., Baldwin, E. and Richard, D. W., Jr. Measurement of cardiac output in man using the technique of catheterization of the right auricle or ventricle. *J. Clin. Invest.*, 24: 106, 1945.
11. Hamilton, W. F. Pressure relations in the pulmonary circuit. *Proc. Soc. Adv. Sc.*, 13: 324, 1940.
12. Carral, R. Variaciones respiratorias de los soplos cardiacos. *Arch. Inst. cardiol. México*, 17: 478, 1947.
13. Condorelli, L. Atrio e ventricolotensiografia. *Riforma med. Roma*, 16–17: 1, 1951.
14. Wilson, F. N., Johnston, F. D., Cotrim, N. and Rosenbaum, F. F. Relation between the potential variations of the ventricular electrocardiograms in leads from the precordium and the extremities. *Trans. A. Am. Physicians*, 16: 258, 1941.
15. Ferrero, G., Duchosal, P. W., Doret, J. P., Grosguerin, J. and Mastrangelo, E. A. Comparisones entre derivationes epicardiaques et precordiales. Presented at the First World Congress of Cardiology, Paris, 1950.
16. Barbato, E. Estudio electrocardiográfico da activacão ventricular normal o patológico. Sua importancia na interpretacão das chamadas curvas de hipertrofia. Thesis, Sao Paulo, 1952.
17. Cisneros, F., Fishleder, B. and Sodi-Pallares, D. Electrocardiograma en algunas lesiones valvulares reumaticas. *Arch. Inst. cardiol. México*, 28: 63, 1958.
18. Avila Cos, L. Apex real y aparente en valvulopatías tricuspídeas. (Maniobra de Rivero-Carvallo y Garza de los Santos.) Thesis, 1958.
19. Fishleder, B. L. Auscultacion y fonocardiografia en la estenosis mitral. *Principia Cardiol. Mex.*, 2: 142, 1955.

Parts I and II of the Symposium on Phonocardiography (Aldo A. Luisada, Guest Editor) appeared in the July and August issues, respectively. Part IV will appear in the October issue and Part V in the November issue.

New Methods

Percutaneous Right Heart Catheterization Using Polyethylene Tubing*

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A PLASTIC TUBE may be passed through a needle in a basilic vein into the right heart and pulmonary artery. Although this simplified method of right heart catheterization has been used intermittently by some investigators during the past thirteen years,[1–3] it has not been widely employed because of the dangers inherent in a technic which does not permit visualization of the catheter tip. When plastic catheters were impregnated with barium sulfate making fluoroscopic visualization possible, mobility was impaired and difficulty was encountered in directing the catheter within the right heart.[4] A technic has been developed for percutaneous, non-fluoroscopic right heart catheterization with polyethylene tubing monitored by the intracardiac electrocardiogram which eliminates the hazards of "blind" catheterization. The present report provides a description of this technic and an evaluation of its use in patients at Grasslands Hospital.

METHOD

A thin-walled 14 gauge needle with stylet was inserted into the basilic vein of either arm after anesthetizing the overlying skin with 1 per cent procaine. A sterile 100 cm. length of polyethylene‡ tubing (inside diameter 0.045 inch, outside diameter 0.062 inch was connected to an infusion of 5 per cent saline through a three-way stopcock. The intracardiac electrocardiogram was obtained by conduction through the saline column, led off to an electrocardiographic monitor from the needle outlet of the saline infusion bottle (Fig. 1). The catheter was then threaded through the needle and advanced slowly into the superior vena cava, right atrium, right ventricle and pulmonary artery under intracardiac electrocardiographic (IC-ECG) control. Since the intra-atrial P wave is deeply inverted in

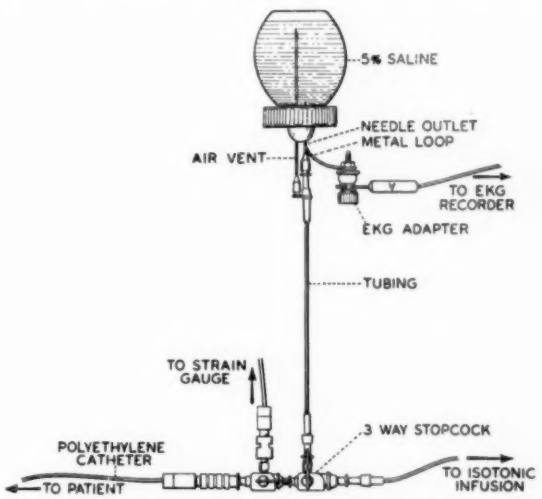

FIG. 1. Arrangement for obtaining the intracardiac electrocardiogram. Conduction proceeds through the 5 per cent saline column, and the electrocardiogram is led off to a monitor from the needle outlet of the saline infusion bottle.

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† Work carried out during tenure of Westchester Tuberculosis and Public Health Association Fellowship. Currently Special Research Fellow, National Heart Institute, U. S. Public Health Service (HF-8347).

‡ PE 160 Intramedic polyethylene tubing, Clay Adams, Inc., New York, New York.

the high right atrium, diphasic in the mid-atrium and upright in the low atrium[5] the position of the catheter tip in the atrium was easily detected by observing the configuration of the P wave (Fig. 2). If the small atrial qrs. complex was replaced by a broad, prominent Q wave followed by a prominent R wave, the appearance of this pattern warned that the catheter resided within the coronary sinus.[5,6] Once the catheter had been advanced to the low atrium, reappearance of the mid- or high atrial patterns indicated coiling within the atrium. The catheter was then withdrawn slightly and readvanced.

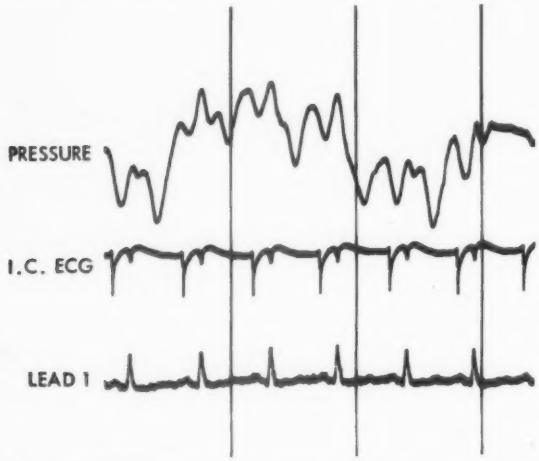

FIG. 2. *Right atrium—polyethylene catheter.* Simultaneous intracardiac electrocardiogram, standard lead I and intra-atrial pressure obtained with the tip of the saline-filled polyethylene catheter in the high right atrium.

The transition from right atrium to right ventricle was readily determined by the appearance of the large voltage rS complex preceded by a diminutive P wave. After the catheter had entered the ventricle, the reappearance of an atrial pattern indicated coiling. If the characteristic rSr′ right ventricular outflow tract pattern was followed by the large rS mid-ventricular pattern, the catheter was withdrawn slightly to prevent coiling within the ventricle.

The small deflections observed as the catheter entered the pulmonary artery were similar to those encountered in the atrium, but distinguishable because of familiarity with intra-atrial configurations gained as the catheter had passed through that chamber in each patient. Verification of the position of the catheter tip within the pulmonary artery was obtained by observation of the pressure pulse on the monitor screen (Fig. 3).

If the "injury pattern,"[7] PQ elevation on the intra-atrial electrocardiogram or ST elevation on the intraventricular electrocardiogram appeared during the procedure, the catheter was assumed to be in contact with the endocardium and it was withdrawn a few millimeters until these segments were again isoelectric, rotated approximately 90 degrees and readvanced.

In withdrawing the catheter even a few millimeters, it is advisable to palpate the catheter at the needle tip, thereby assuring smooth passage beyond the needle point. Alternatively, a blunt needle with a pointed stylet may be introduced into the vein at the beginning of the procedure.

With the catheter in the desired location, an infusion of isotonic solution was then substituted for the 5 per cent saline infusion. Pres-

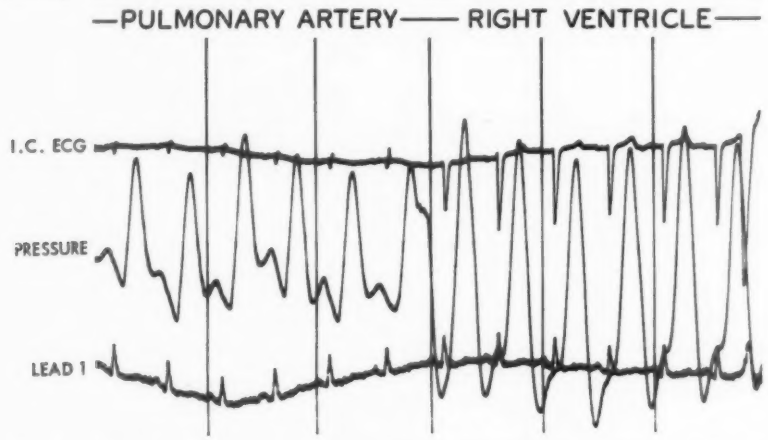

FIG. 3. *Normal pullback—polyethylene catheter.* Simultaneous intracardiac electrocardiogram, standard lead I and pressure obtained as the tip of the saline-filled catheter is withdrawn across the pulmonic valve.

sures were recorded using a Statham strain gauge, and blood samples were taken in the usual manner. During withdrawal of the catheter at the end of the procedure, the 5 per cent saline infusion was again connected, the needle was removed but remained around the catheter, and the catheter was then withdrawn under intracardiac electrocardiographic control. Slight pressure over the vein after removing the catheter achieved hemostasis. Antibiotics were given only to patients with rheumatic heart disease who required antibiotic protection against subacute bacterial endocarditis.

Results

The technic described has been used without serious complications in seventy-five patients. In the last thirty-eight consecutive cases, the pulmonary artery was catheterized in twenty-four patients and the right ventricle in eight. Once the catheter was inserted into the atrium, it entered the pulmonary artery in 75 per cent and the right ventricle in 100 per cent of the cases. Failures were due to inability to place the needle in the vein in a manner sufficient to achieve a forceful flow of venous blood, sharp angulations of the veins at the antecubital fossa or shoulder, or venospasm.

Once the catheter entered the ventricle, if several passes did not locate it within the pulmonary artery, or if ventricular premature contractions occurred after minor manipulation within the ventricle, it was allowed to reside in an electrically quiet situation within the ventricle and no further attempts were made to place it within the pulmonary artery. Cardiac output studies by the Fick and/or dye dilution methods have been carried out in patients at rest and during exercise with the catheter in the ventricle. Ventricular premature contractions were no more frequent with this technic than with the conventional catheterization technic. In one patient a tender cord developed in the antecubital fossa several days after catheterization; in another tenderness was present without any other evidence of inflammation in the area of the venipuncture. In both cases the mild phlebitis subsided promptly when treated with warm soaks.

Comments

Technical Considerations

Certain technical considerations deserve further comment.

Preparation of Catheters: A 100 cm. length of polyethylene tubing was selected in order to permit sufficient length of catheter to remain outside the needle for ease in pressure recording. A slight curve introduced into the catheter at $^3/_4$ inch from the tip by heating over a match assists manipulation into the heart. The proximal end is easily flanged by heat and secured by a plastic tubing adapter.* Connections must be tested for leaks before the catheter is used. Catheters should not be reused because the presence of minute abrasions of the outside wall resulting from repeated manipulation of the catheter may cause venospasm in a subsequent patient. Cold sterilization in a solution of 1:1,000 Detergicide† for thirty minutes is adequate since cultures taken from the catheters and Detergicide solution after this period were sterile. Plastic connector tubing for the strain gauge and infusions may be cold sterilized with the catheters. Catheters may be stored in Detergicide solution ready for use for at least several days, but the catheter must be thoroughly rinsed before it is introduced into the vein. Although polyvinyl tubing may be boiled or autoclaved, it has been found unsuitable for this procedure because it becomes too flexible when warm, and too brittle when cool, to float with the blood stream.

Selecting the Vein and Introducing the Catheter: Although catheterization may occasionally be accomplished through the cephalic vein, angulation of the cephalic vein as it joins the axillary vein imposes the same limitations on the polyethylene technic as on the conventional method with a more rigid catheter. The median cubital or basilic veins are most suitable. The vein should be palpable for about 1 inch beyond the needle, and should proceed from the needle in a straight course for at least this distance. It is unlikely that a polyethylene catheter can be manipulated beyond the needle tip if the vein angulates sharply at this point. In this situation, the needle should not be advanced to the hub, but should be allowed to remain partly outside the skin, although it must be advanced far enough to achieve a forceful flow of venous blood. Occasionally a polyethylene catheter may be advanced beyond a hematoma and into the axillary vein. Difficulty in passing the catheter caused by angulation of a vein does not

* Size C, Clay-Adams, Inc., New York, New York.

† U. S. Catheter and Instrument Company, Glens Falls, New York.

preclude using the analogous contralateral vein. Pain at the site of the catheter tip, while it is being advanced toward the superior vena cava, indicates either that perforation of the venous endothelium has occurred or that the catheter has folded back and is distending the vein; this is an indication for withdrawal of the catheter.

Obtaining the Intracardiac Electrocardiogram: Complete familiarity with the use of the intracardiac electrocardiogram is an essential prerequisite for monitoring non-fluoroscopic catheterization by this technic. Fresh saline solution is used for each patient and is prepared by diluting 100 mEq. of sodium chloride* to 150 cc. of sterile water. No anticoagulant is added to this solution. The standard intravenous infusion sets cannot be used with the 5 per cent saline infusion because of the presence of the reservoir which interrupts the saline column by an air space and consequently prevents transmission of the electrical impulse from the catheter to the electrocardiographic monitor system. If a short needle is used as the outlet, and a longer needle provides an air vent, the appearance of bubbles as air displaces the 5 per cent saline obviates the need for the reservoir. A straight length of infusion tubing is connected to the needle outlet and to the stopcock on the catheter. Abrading $^1/_4$ inch of the needle outlet near the hub with an ampoule file provides a good surface to which a conducting wire may be attached, or a conducting metal loop may be attached to the needle. The wire or loop is then led to the "V" cable of an electrocardiographic monitor. Luisada obtains the intracardiac electrocardiogram by filling the system with 5 per cent saline and leading to the electrocardiographic monitor from the stopcock of the strain gauge.[8]

The Isotonic Infusion: In order to limit the amount of saline administered to a patient, an alternative infusion of 5 per cent glucose and water containing 2 cc. of heparin sodium 1:1,000 and 5 cc. of 20 per cent procaine hydrochloride is also used. To avoid precipitation of procaine base when procaine and heparin are mixed in the same syringe, they are added separately to the liter of isotonic solution. The use of procaine in this infusion has seemed to decrease the incidence of venospasm.

Manipulating the Catheter: Occasionally, the operator perceives the sudden onset of venospasm and finds himself unable to advance the catheter easily. The sudden onset of venospasm is probably of reflex origin, incited by pressure of the catheter against the wall of the vein and is usually relieved when the catheter is withdrawn several inches. Permitting the isotonic infusion containing Novocaine to flush the catheter, tightening a tourniquet around the arm until the vein fills, repositioning the arm between 90 and 180 degrees, turning the head to the opposite side or having the patient inspire deeply, occasionally relieves the venospasm. In two elderly male patients with large, prominent veins, none of these measures was successful and the procedure was abandoned because of venospasm. In no case, however, was there any difficulty in withdrawing the catheter. Repeated, quick, back and forth movement of the catheter is to be avoided since venospasm is more likely to occur under these circumstances.

Duration of the Procedure: A catheter may be left for at least several hours while studies are carried out. For example: a catheter was inserted into the pulmonary artery in the cardiorespiratory laboratory while a preoperative patient was awake. He was then transported to the operating room with the catheter *in situ*, where he was anesthetized and underwent thoracotomy and pneumonectomy for bronchogenic carcinoma. The surgeon palpated the catheter in the anterior branch of the superior branch of the right pulmonary artery. Since the right lung was to be removed, the catheter was withdrawn into the right ventricle where it remained until the end of the procedure. It was withdrawn to the axillary vein after seven hours within the pulmonary artery or right ventricle and served as an intravenous catheter thereafter in the recovery room. Pressures were recorded throughout the procedure. There were occasional ventricular extrasystoles seen on the monitor lead I of the electrocardiogram when the catheter was withdrawn into the ventricle. In dogs, vinyl tubing catheters have been left in place for two weeks and have remained patent without continuous infusion or heparin.[9]

SAFETY AND RELIABILITY

Two factors of critical importance in the evaluation of any proposed modification of conventional cardiac catheterization technics are (1) the safety of the procedure and (2) its reliability.

Safety of the Procedure: Schnabel[4] performed right heart catheterization with vinyl tubing in

* Ionotrate. Abbott Laboratories, Chicago, Illinois.

forty dogs and reported a 25 per cent incidence of subendocardial hemorrhage in the right atrium or ventricle. A mural thrombus was noted in the atrium of one animal, and in another the catheter knotted around a papillary muscle with its tip impinged under a leaflet of the tricuspid valve. Catheter knots have been known to occur in man during left heart catheterization with polyethylene tubing as well as during right heart catheterization with radiopaque catheters. Myocardial perforation is possible with either the conventional catheter[10] or with a flexible plastic catheter which is advanced too forcefully. An x-ray film of a knotted radiopaque catheter in a vein in the arm appears in a recent text on cardiopulmonary physiology.[11] Fatal embolism from a septic thrombus in the right atrium, which formed over a dislodged venous polyethylene catheter, has also been reported.[12]

Despite the rather ominous possibilities of endocardial trauma, catheter knots and dislodged catheters forming the nidus for thrombi and embolization, Schnabel[4] has performed twenty right atrial catheterizations, Fisher[2] has entered the right atrium or pulmonary artery in twenty-five patients and Etsten[3] has measured pulmonary artery pressures in at least four patients using non-fluoroscopic, plastic tubing technics without incident. To date, using the technic described in this report, no untoward effects have resulted from catheterization of the right ventricle or pulmonary artery in fifty-six patients. Therefore, autopsy material is not available for detection of possible resultant endocardial trauma. However, it is unlikely that the risk of such occurrence is any greater than the risk during conventional catheterization with visualization of the catheter tip since the transient injury pattern appears with the same frequency on the intracardiac electrocardiogram during both procedures. Catheter knots have not been encountered. If unsuspected catheter knots have occurred, they have spontaneously become untied since a knotted catheter has never been withdrawn.

The incidence of extrasystoles is approximately the same as with the conventional catheterization method. Special precautions have been taken in withdrawing plastic catheters to prevent shearing the catheters, but even when sharp needles were used, this accident has not occurred. With merely the obvious attention to details attendant to any cardiac catheterization, this technic has proved safe and simple, and it is preferred by those patients who have had a previous conventional right heart catheterization.

Reliability: The use of plastic catheters permits reliable recording of intracardiac and intravascular pressures[13] (Fig. 2). The delay in transmission of a pressure pulse from the catheter tip through the strain gauge system to the electronic recorder used in the present study was found to be 0.006 second, a value which compares favorably with that reported by Gordon and his co-workers[14] for 7F 100 cm. Cournand catheters. In contrast to smaller plastic catheters threaded through 18 gauge needles which permit blood sampling at a rate of only 1 to 4 cc. per minute,[4,15] these larger catheters permit sampling at a rate adequate for cardiac output measurements by the Fick procedure. Electrocardiographic configurations and potentials are in general similar to recordings made from catheters with a tip electrode and wire embedded in the catheter wall, or from conventional radiopaque catheters filled with 5 per cent saline as advocated by Luisada and Liu[8] and Hellerstein and his associates.[16] Some attenuation of voltage is noted, however, when the conducting column has been diluted with blood or isotonic solution.

Percutaneous right heart catheterization has certain distinct advantages over the conventional catheterization procedure. Requiring only a venipuncture rather than a cutdown, percutaneous catheterization is indicated for routine catheterization of adults without congenital heart disease. Fluoroscopy is unnecessary, veins are preserved and the time expended in performing the procedure is lessened. However, the procedure is not applicable to diagnostic catheterizations when visualization of the catheter tip is an important part of the procedure. It is unsuited for children and adults with inaccessible veins and is not recommended for those inexperienced in the interpretation of of the intracardiac electrocardiograms. It is contraindicated in patients who cannot tolerate the intravenous administration of 150 cc. of 5 per cent saline.

Summary

A polyethylene tube may be passed through a thin-walled 14 gauge needle in a basilic vein into the right heart and pulmonary artery using intracardiac electrocardiographic control. The technic described is considered safe for use in

man since the intracardiac electrocardiogram affords chamber localization, advises of location of the catheter tip within the coronary sinus, warns of contact of the catheter tip with the endocardium and detects catheter coiling when the usual sequence of electrocardiographic patterns is reversed as the catheter is advanced. This method is not applicable when visualization of the catheter tip is important for diagnostic purposes; it is more liable to limitation by the anatomy of the veins of the arm than a procedure performed with a more rigid catheter; and it is contraindicated in patients who cannot tolerate the intravenous administration of 150 cc. of 5 per cent saline. It has distinct advantages in selected cases, however, because it replaces a cutdown with a venipuncture, eliminates fluoroscopy and makes repeated catheterization possible through the same vein.

References

1. Sharpey-Schafer, E. P. Personal communication.
2. Fisher, D. L. Retrograde arterial left heart catheterization with nonfluoroscopic venous right heart catheterization. *Proc. Am. Heart Assoc.*, Oct., 1957, p. 35.
3. Etsten, B., Reynolds, R. N. and Li, T. H. The effects of controlled respiration on circulation during cyclopropane anesthesia. *Anesthesiology*, 16: 365, 1955.
4. Schnabel, T. G., Jr., Fitzpatrick, H. F. and Peterson, L. H. A technic of vascular catheterization with small plastic catheters: Its utilization to measure the arterial pulse wave velocity in man. *Circulation*, 5: 257, 1952.
5. Bertrand, C. A., Zohman, L. R. and Williams, M. H., Jr. Intracardiac electrocardiography in man. *Am. J. Med.*, 26: 534, 1959.
6. Levine, H. D. and Goodale, W. T. Studies in intracardiac electrocardiography in man. *Circulation*, 2: 48, 1950.
7. Hellerstein, H. K. and Katz, L. N. The electrical effects of injury at various myocardial locations. *Am. Heart J.*, 36: 184, 1948.
8. Luisada, A. A. and Liu, C. K. Simple methods for recording intracardiac electrocardiograms and phonocardiograms during left or right heart catheterization. *Am. Heart J.*, 54: 531, 1957.
9. Rudolph, A. M. and Paul, M. H. Chronic catheterization of pulmonary and systemic circulations: A technique for repeated measurement of cardiac output and pulmonary and systemic pressures in the unanesthetized dog. *J. Appl. Physiol.*, 10: 327, 1957.
10. Scebat, L., Renais, J., Meers-Bithe, L. and Lenegre, J. Accidents, indications et contre-indications du catheterisme des cavites droites du coeur. *Arch. mal. coeur*, 10: 943, 1957.
11. Gordon, B. L. (ed.) Clinical Cardiopulmonary Physiology, p. 160. New York, 1957. Grune & Stratton.
12. Ayers, W. B. Fatal intracardiac embolization from indwelling intravenous polyethylene catheter. *Arch. Surg.*, 75: 259, 1957.
13. Arst, D. B., Silver, M. and Lahey, W. J. The use of vinyl plastic tubing in recording pressure phenomena. *Am. Heart J.*, 42: 746, 1951.
14. Gordon, A. J., Braunwald, E., Moscovitz, H. L. and Amram, S. S. Delay in transmission of a pressure impulse through a cardiac catheter and vinyl plastic tubing. *J. Appl. Physiol.*, 8: 573, 1956.
15. Fitzpatrick, H. F., Schnabel, G., Jr. and Peterson, L. H. A small plastic tubing technique for right and left heart catheterization. *Fed. Proc.*, 8: 46, 1949.
16. Hellerstein, H. K., Pritchard, W. H. and Lewis, R. L. Recording of intracavitary potentials through a single lumen saline filled catheter. *Proc. Soc. Exper. Biol. & Med.*, 71: 58, 1949.

Seminar on Ballistocardiography*

The Ballistocardiogram in Functional Heart Disease†

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AS A CLINICIAN, I feel that the prompt and proper diagnosis of heart disease still remains a challenge. That our methods, to date, are inadequate to this task is attested by the frequent instance of sudden death when all the usual diagnostic procedures, including the electrocardiogram, have declared the patient "normal." Obviously, some other, at least supplementary, approach to the problem is desirable. It would seem logical that a dynamic evaluation of the heart beat as attempted by the ballistocardiograph should offer a more competent index of the state of the heart than any antecedent electrical current that may stimulate the heart to beat but say nothing of the nature of the beat.

Early studies in the field of ballistocardiography pointed up certain apparently insoluble factors: (1) the physiologic deterioration in aging;[1] (2) the attenuation or distortion of cardiac dynamics by indeterminate factors intervening between the initiating heart beat and the final body movement; (3) the frequent irreconcilability of recorded deterioration with the apparent well-being of the subject; (4) the occasional inconsistency of recordings in the same individual; and (5) the inability to establish any one specific component of the ballistic pattern to correlate with intrinsic myocardial damage.

METHOD

For a practitioner whose only aim was to render this method feasible as an item of office practice, the problem seemed much too difficult. The more precise forms of instrumentation, such as the high-, low- and ultra-low frequency beds could hardly represent the tools of an office procedure. A much more practicable form of instrumentation was that of the photoelectric and electromagnetic direct body technics of Dock.[2] To be sure, these are crude measuring devices particularly when one regards absolute quantitation of cardiac force as the ideal to be achieved. Until such time, however, a comparative qualitative approach may render certain deductions of value, if one accepts that whatever intrinsic errors may exist in the technic—because the approach is comparative—may be regarded as a relative constant. If this thinking carries validity, the direct body technic may be of inestimable value, first, because of the ease of its applicability and, second, because of its potential as a supplementary tool to existing diagnostic methods.

Further refinements have made it possible to differentiate the body movement into its components of displacement, velocity and acceleration[3–5] and thereby establish sharper delineations of the character of these movements. While the components bear a definite mathematical relation to one another, my interest is not in their absolute quantitation but in their distinctive qualitative configurations. The relative position of this technic to that of other

* This issue contains Part XII of the Seminar on Ballistocardiography (edited by Sidney R. Arbeit, M.D., F.A.C.C.). A schedule of the articles already published in this seminar may be found on pp. 101–102 of the January 1959 issue (Vol. III, No. 1). Part XIII, the conclusion of the seminar, will appear in the October issue, with the following articles: A Clinician's Approach to the Ballistocardiogram, EDWARD W. BIXBY, JR., *and* Summary and Conclusions, SIDNEY R. ARBEIT.

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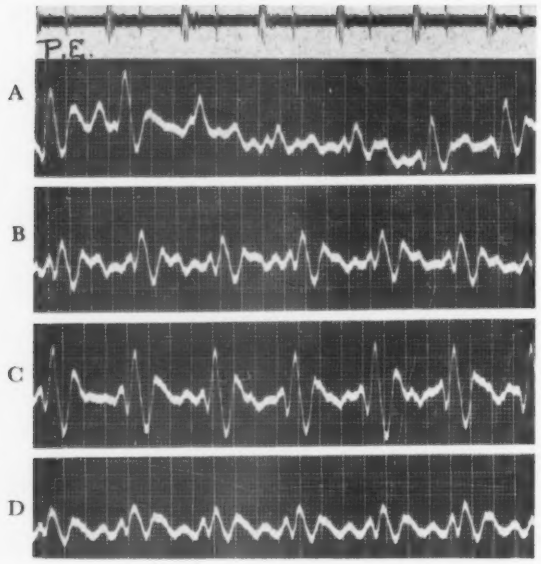


FIG. 1. The effect of respiration on the ballistocardiogram. A, relaxed breathing. B, suspended mid-inspiration. C, deep inspiration. D, expiration. Note that suspended mid-inspiration (B) corrects the aberrations of the expiratory phase of relaxed breathing. This effect is accentuated in deep inspiration (C).

modes of instrumentation has been covered by Talbot[6] in a preceding section of this Seminar. This method which I use makes it possible to record frequencies in a higher frequency range up to 20 or more cycles per second. While the ultra-low frequency bed detects such frequencies, it also simultaneously records frequencies of a much lower range. This fact may be a disadvantage in that this obscures the very frequencies which are being sought.[7]

PROPOSED THESIS

On the basis of a series of observations made with the various forms of photoelectric and electromagnetic direct body technics, I would like to offer a revised basis for the interpretation of the ballistocardiogram. Summarized, it is as follows: (1) the need to differentiate functional deterioration of vascular origin from that of organic myocardial origin and to properly evaluate the role of respiration; (2) the importance of inspecting all three components of body movement—displacement, velocity and acceleration—and evaluating each in the light of the other two; (3) the need to study the character of HI, particularly that inscribed in acceleration, because it represents the initial phase of myocardial contraction; and (4) the value of recording the higher frequency range of body movement, in order to delineate the nature of this tracing more clearly.

SIGNIFICANCE OF NON-ORGANIC BCG DETERIORATION

In the early period, many tried to correlate the degree of deterioration of the ballistocardiographic pattern with the organic deteri-

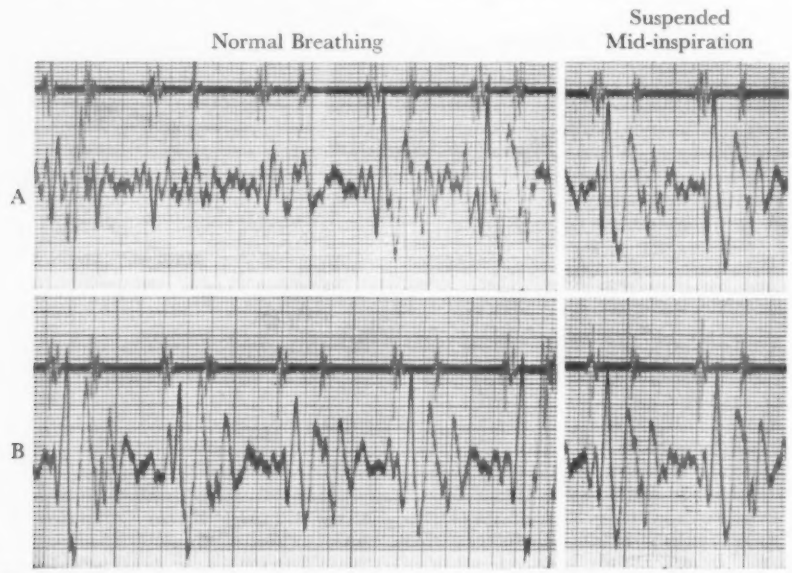


FIG. 2. The effect of suspended mid-inspiration and the abdominal binder on the aberrations of the ballistocardiogram in relaxed breathing. A, without abdominal binder. B, with binder. Note that the two are comparable in their correction both in amplitude and HI configuration.

oration of the myocardium,[8] and a method of gradation was established. It soon became obvious, however, that grade 4 was not necessarily an omen of impending death, particularly when it was a function of aging. Another challenging group is represented by the young asthenic individual who frequently complains of precordial pains. These patients often show varying degrees of ballistocardiographic deterioration out of proportion to what one would expect on the basis of age. In addition, some of them may present electrocardiographic changes following exercise that may cause an organic basis of the complaints to be suspect. In this group, then, both methods could be misleading. Obviously, the disturbances are functional and it is my thesis that they are attributable to the severe degree of splanchnic pooling to which these individuals are prone. This principle can be established ballistocardiographically by the specific approach I have established for myself.

THE ROLE OF RESPIRATION

Before going into its discussion, certain correlations between respiration and cardiac volume output, as already described by Brown et al.[9] should be re-emphasized. Deep inspiration increases the intrathoracic negative pressure, increasing the volume of venous return to the right side of the heart, thereby increasing cardiac output. Expiration acts conversely. The large output differences between the two phases are counteracted by the existence of the "pulmonic pool" which acts as the buffer from which the left ventricle can draw. It has also been observed that suspended mid-inspiration will maintain a stable series of patterns and base-line in the low frequency table technic. However, since this entails the hazards of Valsalva and Mueller effects it has been ignored by many.

THE ROLE OF "SPLANCHNIC POOLING": THE VALUE OF SUSPENDED MID-INSPIRATION

In my early experience, patients were routinely studied in all four phases of respiration. With other observers, I was frequently impressed with the fact that in some patients in whom rather large ballistocardiographic deteriorations occurred during relaxed breathing, these changes were promptly restored toward normal by suspending breathing in mid-inspiration or by deep inspiration (Fig. 1). It was similarly observed that the same

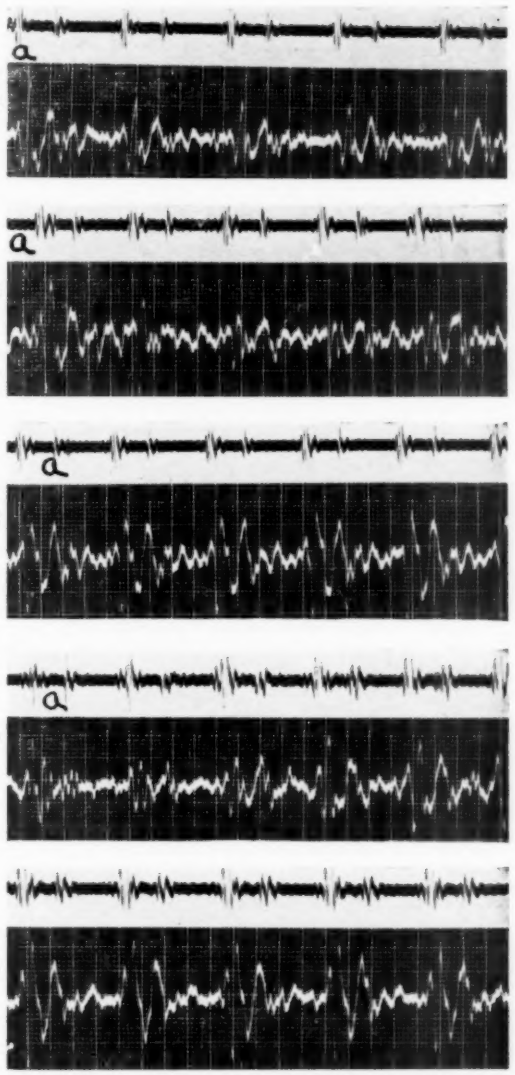


FIG. 3. Case 1. Determination of "functional" rather than "organic" deterioration of the ballistocardiogram following exercise. All tracings are direct body acceleration ballistocardiograms. A, normal breathing (control). B, breathing after exercise. C, suspended mid-inspiration after exercise. D, at rest, thirteen days later. E, suspended mid-inspiration (resting) immediately after (D). The correction to normal of the abnormal ballistocardiogram by suspending breathing establishes the functional character of the ballistocardiogram abnormality.

result could be achieved even during relaxed breathing by applying a binder to the abdomen (Fig. 2). It soon became obvious that recording during relaxed breathing and suspended mid-inspiration alone would provide all the required information.

CASE 1. This is dramatically demonstrated in the unusually instructive case of a fifty-one year old man with neurasthenia who complained of marked

weakness, cold sweats, dizziness and tachycardia. He had a previous history of myocardial infarction occurring fifteen years earlier from which he was, supposedly, completely recovered.

Physical examination showed marked orthostatic hypotension. A control electrocardiogram was normal as was his ballistocardiogram (Fig. 3A), both taken during relaxed breathing and suspended mid-inspiration. Following a single exercise test, the electrocardiogram showed ST deviations suggestive of mild ischemia, while the ballistocardiogram showed severe deterioration (Fig. 3B). This finding in itself would have suggested an organic cause for the electrocardiographic changes, were it not immediately corrected by suspended mid-inspiration (Fig. 3C). Thirteen days later, the patient returned for a repeat examination. At this time, while the control electrocardiogram was again normal, the resting ballistocardiogram now showed severe deterioration (Fig. 3D), which again was restored by suspended mid-inspiration (Fig. 3E).

Comment: The functional aspects of the entire problem were obvious in spite of grounds for "organic" deterioration with the patient's previous "coronary" history. The controlling factor in the diagnosis, however, both in regard to the deterioration following exercise in the first examination and the deterioration at rest in the second examination, was the comparable restoration in both instances by suspending breathing in mid-inspiration.

It is well to make a sharp distinction between mid-inspiration and deep inspiration. The latter produces an extremely negative intrathoracic pressure resulting in a marked increase in venous return to the right side of the heart that possibly vitiates what might have persisted as an alteration of organic significance. The chances of doing this in the mid-phase of respiration are considerably less.

THE ROLE OF THE VASCULAR TREE: THE EFFECT OF DRUGS

The peripheral vascular system can also play a large role in determining the form of the ballistocardiographic pattern. When the contribution of this portion of the cardiovascular system is eliminated by drugs, it is possible to visualize the intact central "pump."

CASE 2. To illustrate this point, I present the case of a twenty-eight year old woman with neurasthenia whose presenting complaints were faintness, dizziness, palpitations and precordial twinges of pain. She smoked from one to two packs of cigarettes a day. On examination, she presented "orthostatic hypotension"—without hypotension but with marked tachycardia in changing from the prone to the upright position. A comparative study employed the photoelectric cell: at rest, following smoking and following intravenous administration of certain ergot derivatives (Fig. 4).

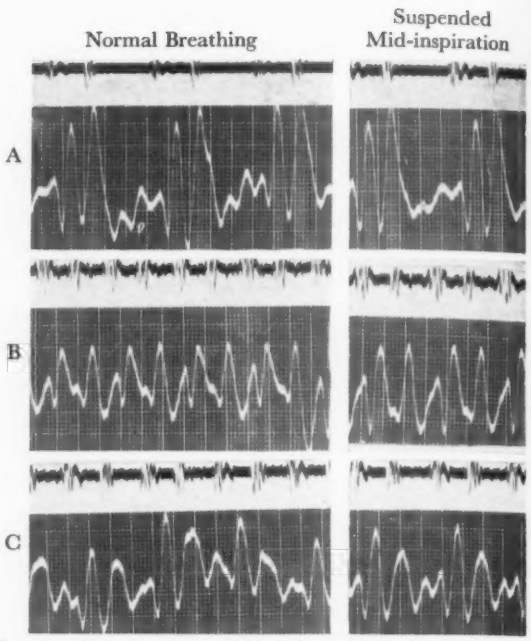


FIG. 4. Case 2. The ability of certain drugs to correct the abnormal ballistocardiogram through their action on the blood vessels. An unusual resting curve (A) in a twenty-eight year old woman with neurasthenia shows the anticipated effect of smoking (B) which is only partially corrected by suspended mid-inspiration but is completely corrected even beyond that of the control by the intravenous administration of dihydroergocornine, dehydroergocryptine and dehydroergocristine (C). (Records recorded by direct body photoelectric ballistocardiogram.)

The resting control record was, in itself, interesting because while HI was normal in amplitude and configuration, IJK was of unusually high amplitude and short duration and was followed by an L wave of even greater amplitude and equally short duration (Fig. 4A). Smoking induced the anticipated effects of tachycardia and ballistocardiographic deterioration[10] characterized by over-all diminution in amplitude with HI merging ascendingly on IJ (Fig. 4B). However, the intravenous injection of combined *dihydroergocornine, dihydroergocryptine and dihydroergocristine*,[11,12] which acts particularly on the terminal myoneural junctions of the arterioles, produced prompt restoration of the ballistocardiographic complex to a pattern even more characteristically normal than that of the control (Fig. 4C).

Comment: This case serves to emphasize further the large role the vascular element can play in the determination of the ballistocardiographic pattern apart from the possi-

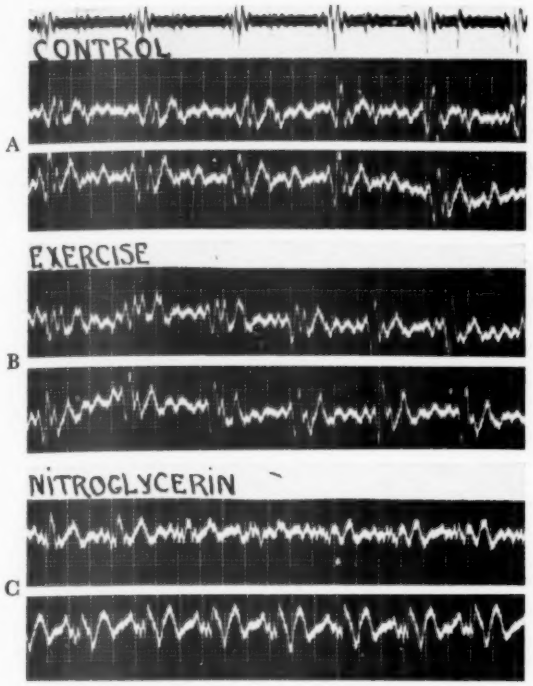


FIG. 5. Case 3. Records in each group taken during normal breathing (*top row*) and during suspended mid-inspiration (*bottom row*). A, at rest. B, after exercise. C, following administration of 0.6 mg. nitroglycerin. The abnormality in the control tracing is completely corrected by suspended mid-inspiration as is that after exercise. However, although the decreased amplitude caused by nitroglycerin is corrected by suspended mid-inspiration the HI abnormality persists. All tracing are direct body acceleration curves taken with the Elliott mercury accelerometer.

bility of any cardiogenic factor. In fact, in such instances, the assumption seems safe that the heart itself is organically completely sound.

Nitroglycerin is another drug that points up this vascular component. Starr[13] has recently reported an alteration in the HI wave in about 50 per cent of the cases in which nitroglycerin was administered. This has been much in accord with my own observations. The change has been particularly striking in acceleration when HI becomes little more than a vibratory complex.

CASE 3. The foregoing is well demonstrated in a forty-three year old man with neurasthenia in whom a comparative study was carried out employing the Elliott mercury accelerometer: at rest, following exercise and following the administration of nitroglycerin, both during relaxed breathing and suspended mid-inspiration (Fig. 5). This instrument records the same function of motion as does the direct body electromagnetic ballistocardiograph whose signal is differentiated to acceleration.

At rest and following exercise, the records were completely normal in both respiratory phases. Following the administration of nitroglycerin, there was marked deterioration during relaxed breathing—both in amplitude and HI configuration. When breathing was suspended in mid-inspiration, however, there was restoration in amplitude but, surprisingly, no improvement in HI configuration.

Comment: Here again, I believe we are dealing primarily with the effect of the drug in producing "splanchnic pooling," thereby markedly diminishing the circulating volume return. As to the unusual failure of HI to be corrected by this same maneuver, there seem to be grounds for the speculation which will be attempted later. We appear, then, to be dealing with a factor other than the myocardium that plays a dominant role in the determination of the eventual pattern, namely, the vascular component of the cardiovascular system. The location of the blood mass can strongly influence, if not determine, the final pattern of the cardiac dynamics.

THE SIGNIFICANCE OF THE HI WAVE

FUNCTIONAL DETERIORATION

One cannot lay down criteria for functional disturbances of the cardiovascular system without attempting to establish (1) those which are of organic significance and (2) the specific components of the pattern with which one should be most concerned. The aforementioned uncorrectable effect of nitroglycerin administration on the HI component highlights the question of its significance in the overall pattern. Is it this or the J wave or is it the entire ballistocardiographic complex that must be most carefully observed to detect myocardial impairment? I believe that it is the HI component that merits most study. The cadaver experiments of Starr[14,15] have already emphasized the relationship between the amplitude and slope of HIJ on the one hand with the acceleration of the plunger on the other. This is in accord with my own experience.

I further believe that the most significant data are contained in the HI component recorded in acceleration rather than that recorded in velocity or displacement. Because of its greater sensitivity, what might otherwise be labeled as "organic" by the latter two may be shown to be completely "functional" by the first.

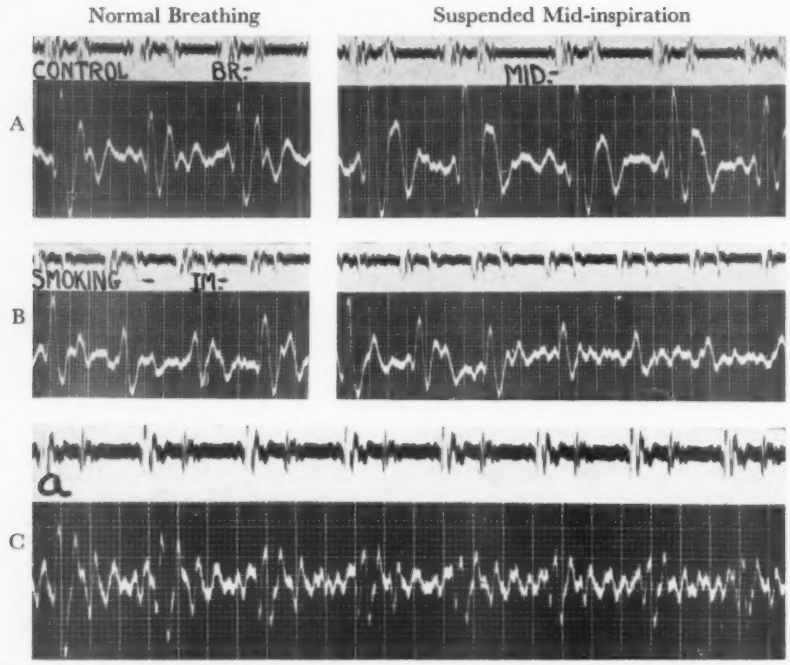


FIG. 6. Case 4. The deterioration of the direct body displacement ballistocardiogram by suspended mid-inspiration in a case of pectus excavatum. This is believed due to the exhaustion of the "pulmonic pool." A, control ballistocardiogram during relaxed breathing (BR) and suspended mid-inspiration (Mid). B, immediately after smoking during relaxed breathing and suspended mid-inspiration. C, acceleration tracings recorded at same time as (B) during suspended mid-inspiration. Note that the tendency to deterioration of the ballistocardiogram is accentuated by smoking (B) and that while HI shows progressive deterioration in displacement (B) it improved in acceleration (C).

CASE 4. This is demonstrated in a forty-three year old man with pectus excavatum who complained of undue dyspnea on climbing stairs and of frequent brief precordial pains. He smoked one pack of cigarettes a day. There was electrocardiographic and roentgenographic evidence of some displacement and rotation of the heart.

While the ballistocardiographic record in relaxed breathing (Fig. 6A) showed no significant abnormality, in suspended mid-inspiration it revealed a slow progressive decline in amplitude of the ballistocardiographic patterns. Smoking (Fig. 6B) further accentuated this tendency, with the last complex in displacement strongly resembling a grade 4 deterioration. Of striking interest, however, was that while HI was showing this progressive deterioration in the displacement record, merging ascendingly in IJ with accompanying diminution in amplitude, the acceleration record (Fig. 6C) showed progressive improvement and delineation of HI despite the accompanying comparable diminution in amplitude.

Comment: This case emphasizes that what one would have rightfully read as organic deterioration on the basis of the direct body displacement ballistocardiographic record is simply an alteration of functional origin. In this instance, it is most likely due to the rapid progressive exhaustion of the "pulmonic pool" during suspended mid-inspiration—already depleted by the physical compression of the thoracic cage.

ORGANIC DETERIORATION

Early Myocardial Infarction with Pain and an Abnormal Electrocardiogram: The following is an illustrative case.

CASE 5. A forty-nine year old man of average build complained of sporadic precordial pains of varying duration and intensity. This patient remained ambulatory and I was able to follow him serially over the next ten days. The initial resting electrocardiogram might have been passed as normal except for some slight ST-T alteration in lead III (Fig. 7A). The second and third electrocardiograms, however, showed progressive deepening of Q_3 with a similar pattern in aVF suggesting posterior wall infarction (Fig. 7A). The precordial leads were unaltered.

The comparative ballistocardiographic recordings

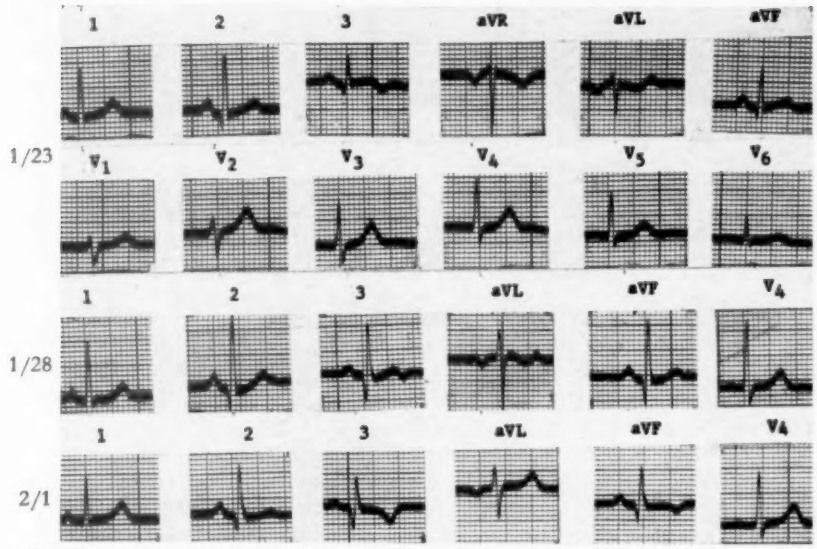


FIG. 7A. Case 5. Electrocardiographic records show progressive evolution of posterior wall myocardial infarction.

were of great interest. Comparing the displacement ballistocardiogram at the time of the first examination with that of the third (Fig. 7B), it was found that while the first showed diminution in the amplitude of the over-all patterns with deterioration of HI and merging of it with the ascending IJ, displacement in the third ballistocardiogram showed complete restoration of both amplitude and configuration. In acceleration, however, while the first examination showed similar diminution in amplitude with comparable deterioration of HI, the abnormal HI persisted in its deteriorated state, despite restored amplitude in the third record (Fig. 7C).

This study was repeated six weeks later following two weeks of bed rest and four weeks of increasing activity. While the electrocardiogram continued to present the Q_3T_3 pattern of posterior wall infarction, the ballistocardiogram in displacement (Fig. 7D) presented the typical pattern of asthenia-deterioration during relaxed breathing corrected by suspended mid-inspiration, while in acceleration relatively normal patterns occurred in both respiratory phases.

Comment: This case stresses several points; first, the relation of the ballistocardiogram to the early phase of acute injury and, second, its value in convalescence. In the first instance, emphasis is placed on the progressive improvement in cardiac dynamics in the face of electrocardiographic retrogression and the persistence of HI deterioration in acceleration compared

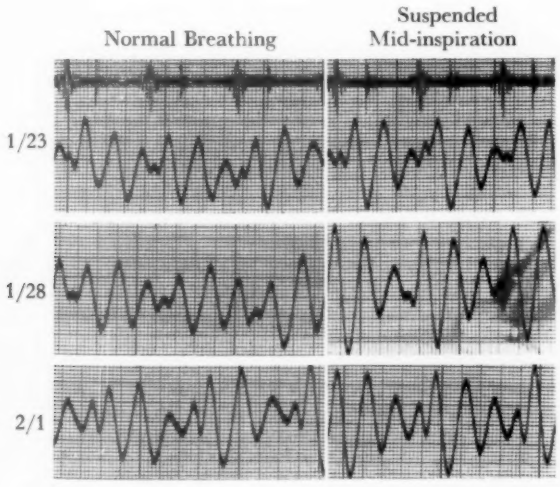


FIG. 7B. Case 5. The effect of early myocardial infarction on the ballistocardiogram. Displacement ballistocardiogram taken on same dates as in Figure 7A.

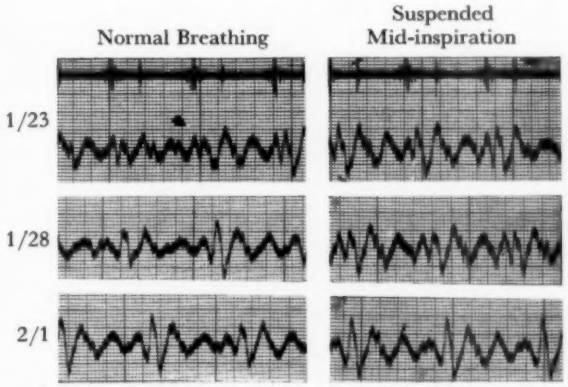


FIG. 7C. Case 5. Acceleration ballistocardiogram taken on same dates as in Figures 7A and 7B.

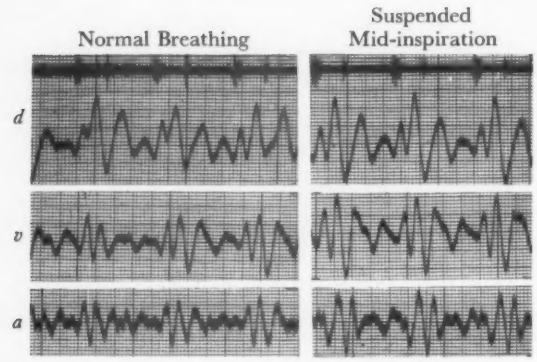


FIG. 7D. Case 5. Ballistocardiogram (*d,v,a*) taken six weeks later. Note that the greatest ballistocardiogram deterioration in the initial records is in the configuration of HI in all components of movement (7B, 7C) in spite of ample amplitude of the over-all pattern and in the face of inconclusive alteration of simultaneously recorded electrocardiogram. Thereafter, there is improvement of the ballistocardiogram as the electrocardiogram shows progressive changes. The ballistocardiogram taken six weeks later (7D) shows relatively good HI particularly in acceleration confirming the satisfactory convalescence.

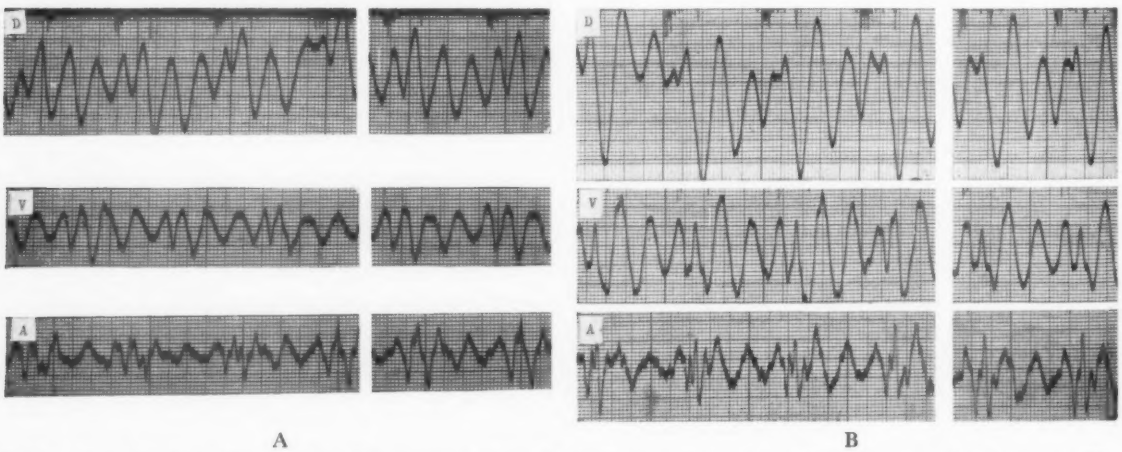
with that in displacement in reflecting more competently the still existing state of myocardial damage. In the second instance, repeated recordings helped to determine the state of convalescence and the degree of permissible activity.

Early Myocardial Infarction with no Pain and no "Specific" Alterations in the Electrocardiogram: Up to this point, the challenge was made easier by the clinical observation of precordial pains, however slight, that accompanied the electrocardiographic changes. The challenge becomes much greater when pain is absent or, at best, only suggestive. This is demonstrated in two cases.

CASE 6. The first case is that of a fifty-one year old man of sthenic status and hyperdynamic personality. I had seen him periodically over the course of the previous year for sporadic complaints of precordial pains associated with diastolic hypertension of 140–150/100–110 mm. Hg. The electrocardiograms at rest were normal, but following exercise showed slight ST_3 depression and diminution in amplitude of the T waves in V_4. In the ballistocardiogram the amplitudes of the over-all patterns in all three components of movement were diminished (Fig. 8A). HI in displacement was distinctly abnormal in both respiratory phases of relaxed breathing and suspended mid-inspiration; that in acceleration was of relatively good configuration in both phases.

This study was repeated two months later (Fig. 8B) following therapy with pentaerythritol tetranitrate and Raudixin with restoration of a normal pressure reading of 130/80. Repeat electrocardiograms were normal even after exercise. Ballistocardiographically while the pattern amplitudes showed marked improvement generally, the HI of displacement continued in its deteriorated state of diminished amplitude high on the ascending limb of J (Fig. 8B). In acceleration, however, HI was of good amplitude and configuration, reflecting the organically improved state of the myocardium.

This patient was again seen one year later after he had been awakened from sleep by nausea and dizziness following a long day in a prolonged head-down position, while painting the roof of his house. Thirty-six hours later, he showed dizziness and orthostatic hypotension. The electrocardiogram (April 23, 1957) was entirely normal, although the T waves showed diminution in amplitude two



A B

FIG 8. Case 6. The effect of diastolic hypertension on the ballistocardiogram and improvement with therapy. The diminished amplitudes and configurations of the ballistocardiogram (A), are improved after therapy. B, note, however, the poor HI of displacement despite markedly improved amplitude but its complete restoration in acceleration.

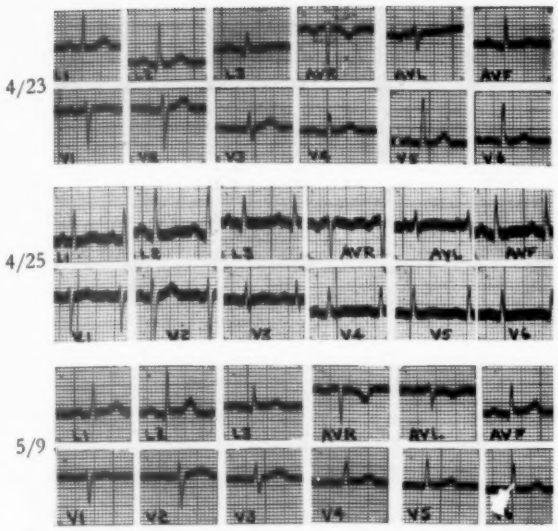


FIG. 9. Case 6. Serial electrocardiogram tracings one year later show only minor T wave changes.

days later (April 25) (Fig. 9). Ballistocardiographically, while the HI of displacement remained identical with that of the previous year in both phases of breathing, that of acceleration showed distinct deterioration (Fig. 10). All initial laboratory examinations including blood count, sedimentation rate and serum transaminase were normal. In spite of all this my clinical impression was that the patient had suffered a myocardial infarction. On the third day, the white cell count rose sharply as did the sedimentation rate to a peak of 76 mm./hour. On the eighth day the serum transaminase, similarly, became moderately positive. While an interim electrocardiogram (April 25) showed no "specific" change,

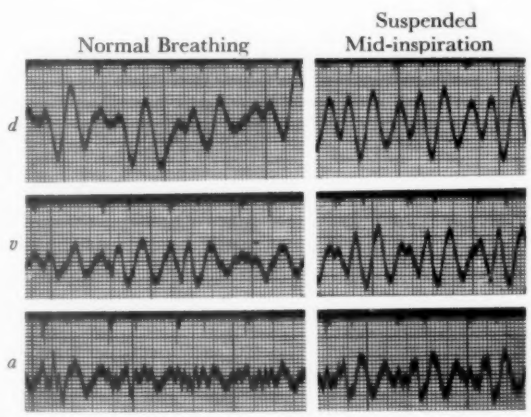


FIG. 10. Case 6. Detection of silent myocardial infarction by the ballistocardiogram. Ballistocardiogram on April 23, 1957, at time of first electrocardiogram in Figure 9. Note the marked deterioration of the direct body acceleration ballistocardiogram. This is not corrected by suspended mid-inspiration although the displacement and velocity curves improve.

one taken on the seventeenth day (May 9) showed inversion of T in aVL while the T waves that previously showed diminished amplitudes were completely restored to normal (Fig. 9). The diagnosis of acute myocardial infarction seemed adequately corroborated despite only minor electrocardiographic changes. The patient has returned to full duty and is well one year later.

CASE 7. The second case is that of a fifty-two year old man of average stature who, without premonitory symptoms, suddenly "collapsed" while walking in the neighborhood of the hospital. The serum transaminase showed marked elevation (over 190 units) on the second day, arousing the clinical suspicion of myocardial infarction in spite of a normal electrocardiogram (Fig. 11) which persisted throughout his hospital course.

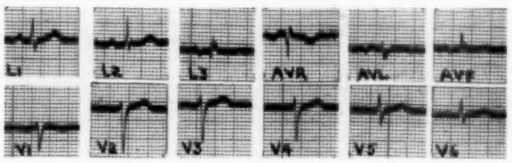


FIG. 11. Case 7. Normal electrocardiogram on admission to hospital (April 9, 1957). Serial tracings on April 19 and May 24 showed no change.

An acceleration ballistocardiogram (Fig. 12A) taken after admission showed distinct HI deterioration in acceleration in both phases of breathing. This was definitely improved in a subsequent record taken 10 days later (Fig. 12B). The patient's condition was treated as a myocardial infarction and he had an uneventful recovery. A repeat study six weeks later (Fig. 12C), while the patient was ambulatory, showed HI to be still normal in configuration.

The Relative Significance of the Form of HI Compared with Its Amplitude: This last study raised the problem of the relative significance of pattern amplitude as a reflection of the myocardial state compared with the form of the initial acceleration of the cardiac contraction, regardless of amplitude. Certainly, the amplitudes of the J and L waves of the first two examinations in Case 7 (Fig. 12) were considerable and of relatively normal configuration in spite of the evidence of early myocardial damage reflected by HI deterioration. In addition, on the third examination, when the patient was relatively well, the amplitudes were quite diminished although HI, in itself, was relatively normal in configuration. This observation was previously emphasized in Case 6 in which the configuration of HI labeled the problem "functional" on the first examination—although the amplitudes were then

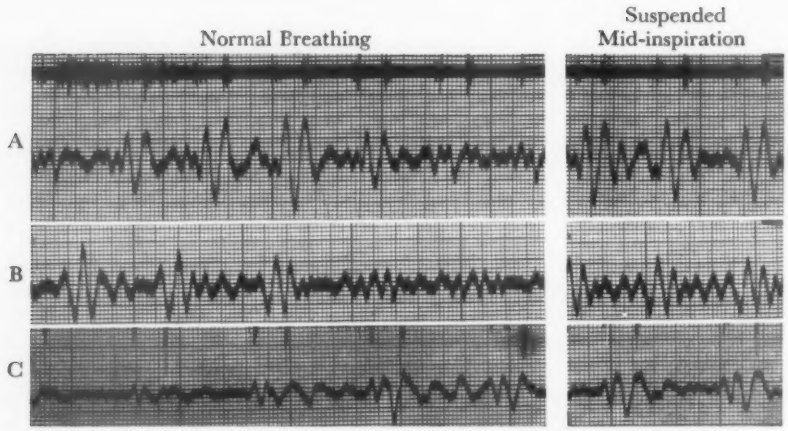


FIG. 12. Case 7. Correlated acceleration tracings. The detection of silent myocardial infarct by the ballistocardiogram. A, abnormal ballistocardiogram on admission, only partially corrected by suspended mid-inspiration. B and C, subsequent serial tracings show improvement particularly in suspended mid-inspiration. A, on admission. B, ten days later. C, six weeks later.

all diminished—and "organic" a year later with the amplitudes still comparable. Apparently, the factors responsible for the initial phase of the ballistocardiographic complex must be dissociated from the factors responsible for the latter phase. It is my impression that the former is related to the more significant portion of the systolic ejection and the latter dominated by the vascular component beyond the heart.

SIGNIFICANCE OF THE DETERIORATED "VIBRATORY" HI COMPONENT

There are certain conditions that may exert a predominant effect on the first phase—the HI component—as described in myocardial infarction, where HI deterioration assumes the character of a vibratory complex which suspended mid-inspiration does not materially improve, while the remainder of the pattern may or may not be comparably affected. This effect on HI was also noted following nitroglycerin administration and less so, following smoking. The possibility that this "vibratory" complex in all of these may represent a common asynchronous contraction of the ventricles is a strong one. In myocardial infarction this may well be due to the direct effect of "trauma" interfering with the synchronous "timing" of muscle fiber contraction. In the case of smoking this may be due to the alteration in the volume of circulation "effectively" available to the heart following smoking, which is diminished by the generalized vasoconstriction as well as the increased resistance against which the heart must work. The effect following the administration of nitroglycerin may be due to the widespread vasodilatation and "splanchnic pooling." In both instances, both the initial and final phases of the over-all pattern are affected—expressed as HI deterioration in the first and diminution in amplitude in the second.

Suspending breathing in mid-inspiration has only a slight effect on either phase of the deterioration following smoking. Nitroglycerin administration, however, tends to correct the second phase in terms of amplitude but not necessarily the initial, HI, phase of systolic ejection. The rationale follows that the generalized vasoconstriction due to smoking will not easily be affected even by splinting the abdominal wall by suspended mid-inspiration. In the case of nitroglycerin, however, where vascular relaxation and "pooling" result, such splinting will increase the circulating volume return as manifested by the restored amplitude. As to the persistent HI deterioration, however, while it may represent asynchronous contraction of the ventricles, it seems logical to regard it as secondary to the profound effect on the vascular bed. The possibility that smoking and nitroglycerin can directly affect the muscle fibers of the heart and so upset their synchronous contraction may still exist.

DETERMINATION OF FUNCTIONAL SIGNIFICANCE OF ELECTROCARDIOGRAPHIC ABNORMALITIES

This brings us to the problem of the young person with neurasthenia who has variable,

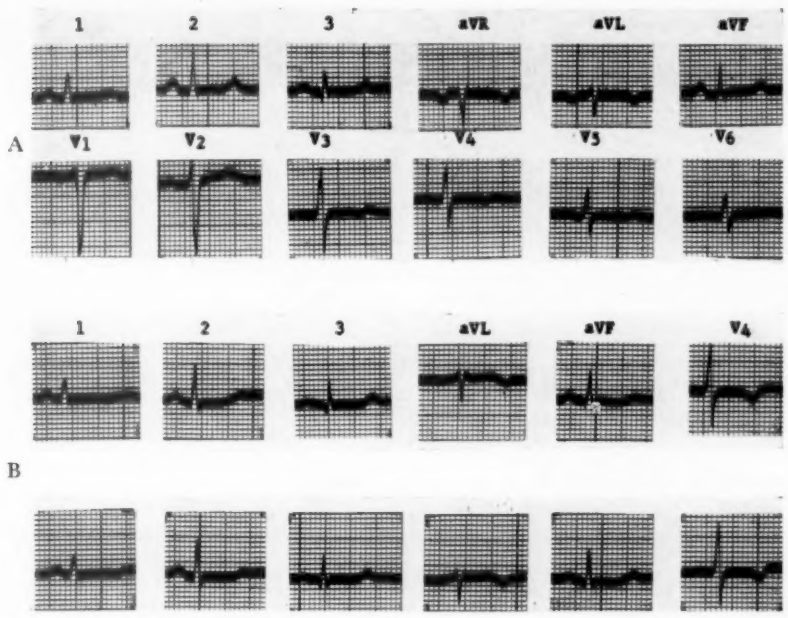


FIG. 13. Case 8. Electrocardiogram of a thirty-nine year old woman with neurasthenia showing minor ST and T changes at rest A, becoming more marked after standard exercise test. B, top tracing is immediately after exercise; lower tracing is two minutes after exercise.

vague, complaints of precordial pains. These pains are generally of short duration although some are more enduring, with or without radiation, and are associated with feelings of fatigue and debilitation. The blood pressures may be normal or low and the electrocardiograms normal or abnormal.

CASE 8. This group is illustrated by the case of a tall thirty-nine year old woman with all of these complaints. The resting electrocardiogram showed inversions of T in a VL and V_4 and diphasic T in V_3 (Fig. 13A). Following a standard exercise test (Fig. 13B) there was inversion of T in V_2–V_4 which returned to the resting control after nine minutes. In contrast, the ballistocardiogram was of normal configuration and amplitude in all components of movement, both at rest (Fig. 14A) and following exercise (Fig. 14B). Dependent on this finding indicative of good myocardial function, the patient, already in a state of anxiety, was reassured and encouraged to engage in physical activity in order to improve physical tone. Following a year of this regimen, the patient was again studied. The electrocardiographic abnormalities were found to be identical with those of the previous records although the patient was doing well. This case is of interest because one could justly be impelled to supervise such problems with undue timidity with all the ensuing psychologic implications to the patient.

Finally, there is the question of proper emphasis on the individual functions of movement. Throughout this presentation, I have repeatedly emphasized either displacement or acceleration. Relatively little attention was paid to the velocity tracing. It is my impression that from the qualitative standpoint, which is my approach to the problem of ballistocardiography, velocity has no particular significance other than as a transitional tracing

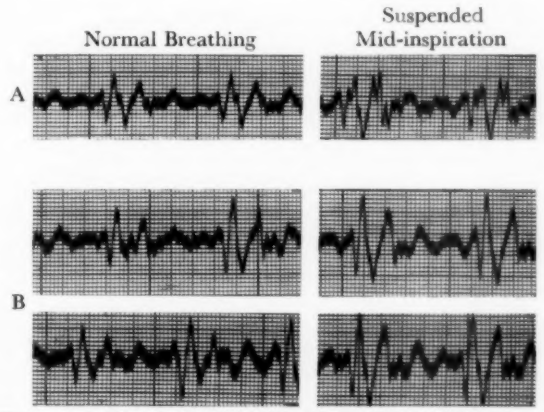


FIG. 14. Case 8. The ballistocardiogram aids in establishing the presence of good myocardial function despite the abnormal electrocardiogram. A, at rest. B, four and nine minutes after exercise. All tracings are normal.

in passing from displacement to acceleration. This particularly applies to the HI component which begins to be recognizable in velocity even though it may be entirely obscured in displacement. In common with the other movement components, suggestive abnormalities during the relaxed breathing phase in "velocity" may be entirely corrected by suspended mid-inspiration, demonstrating their functional origin.

Summary

In summary, I would like to re-emphasize the following concepts:

1. The simple direct body technic recording forces in the single head-foot direction may be a completely practicable method of cardiac evaluation if we understand that we are interested in the comparative, qualitative, variations of the patterns and not in the quantitation of those forces.

2. In recording the forces of a pump that circulates fluid through a static system we must keep in mind that the conduits of this system play as much of a role in the resulting forces recorded as does the pumping mechanism itself.

3. The sites and degree of pooling of the circulating blood may play a dominant role in the determination of the form of the recorded pattern by determining the amount of blood available to the heart.

4. The deteriorating effect of pooling on the pattern may be counteracted by the application of an abdominal binder or the apparently comparable maneuver of suspending breathing in mid-inspiration.

5. The HI component of the direct body acceleration ballistocardiogram appears to be the most significant element in determining the organic state of the myocardium. The deterioration of this component even in the presence of an otherwise normal ballistocardiogram, electrocardiogram or other laboratory studies, may be evidence of an underlying myocardial infarction.

6. The J and L waves may represent, predominantly, the forces within the vascular tree which may be best detected by instrumentation confined to the lower frequency range.

Addendum

Since preparation of this article, another "functional" manifestation has been observed, that of "ischemia." This is characterized by an M-shaped IJK in the face of a normal HI and may represent the prodromal phase of myocardial infarction in the younger individual or fibrosis in the aging.

References

1. Starr, I. and Hildreth, E. H. The effect of aging and of the development of disease on the ballistocardiogram. A study of 80 subjects, originally healthy followed from 10–14 years. *Circulation*, 5: 481, 1952.
2. Dock, W., Mandelbaum, H. and Mandelbaum, R. A. Ballistocardiography. St. Louis, 1953. C. V. Mosby Co.
3. Smith, J. E. and Bryan, S. Studies of frequency response in ballistocardiography. *Am. Heart J.*, 45: 40, 1953.
4. Arbeit, S. R. and Lindner, N. A new full-frequency range calibrated ballistocardiograph; recording body ballistics in displacement, velocity and acceleration. *Am. Heart J.*, 45: 52, 1953.
5. Smith, J. E. and Bryan, S. Simultaneous calibrated recording of displacement, velocity and acceleration in ballistocardiography. *Am. Heart J.*, 45: 715, 1953.
6. Talbot, S. A. Biophysical aspects of ballistocardiography. *Am. J. Cardiol.*, 2: 395, 1958.
7. Noordergraaf, A. Physical Basis of Ballistocardiography. The Hague, 1956. Excelsior.
8. Starr, I. Essay on the ballistocardiogram. *J. A. M. A.*, 155: 1413, 1954.
9. Brown, H. R., de Lalla, V., Epstein, M. A. and Hoffman, M. I. Clinical Ballistocardiography. New York, 1952. MacMillan Co.
10. Caccese, A. and Schrager, A. The effects of cigarette smoking in the ballistocardiogram. *Am. Heart J.*, 42: 589, 1951.
11. Goetz, R. G. and Ames, F. Reflex vasodilatation by body heating in diagnosis of peripheral vascular disorders. *Arch. Int. Med.*, 84: 396, 1949.
12. Goetz, R. H. The effect of intra arterial injections of hydergine and dihydroergocornine on peripheral circulation in man. *Circulation*, 13: 63, 1956.
13. Starr, I., Pederson, E. and Corbascio, A. N. The effect of nitroglycerine on the ballistocardiogram of persons with and without clinical evidence of coronary heart disease. *Circulation*, 12: 588, 1955.
14. Starr, I., Horowitz, O., Mayock, R. I. and Krumbhaer, E. B. Standardization of the ballistocardiogram by simulation of the heart's function at necropsy with a clinical method for the estimation of cardiac strength and normal standards for it. *Circulation*, 1: 1073, 1950.
15. Starr, I. and Schnabel, T. G., Jr. Studies made by simulating systole at necropsy. III. On the genesis of the systolic waves of the ballistocardiogram. *J. Clin. Invest.*, 33: 10, 1954.

Experimental Study

Cardiac Responses to Epinephrine and Norepinephrine During Prolonged Cholesterol and High Fat Feeding in Rabbits*

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FOLLOWING prolonged cholesterol feeding in rabbits, gross and microscopic pathologic changes can be detected in the coronary vessels. The object of this investigation was to assess the functional changes in the heart occurring during the development of these lesions. It was also hoped that from such studies some procedure might be evolved for the objective experimental assessment of drugs affecting the coronary circulation in the intact unanesthetized animal.

In this study injections of either epinephrine or norepinephrine were employed to test the coronary efficiency. Levine, Ernstene and Jacobson[1] have reported that the subcutaneous injection of epinephrine (1 mg.) in man can induce attacks of anginal pain and suggested this procedure as a diagnostic test for angina pectoris. However, Katz, Hamburger and Lev[2] reported that this test was "unreliable and associated with severe reactions." Since the introduction of norepinephrine, significant differences have been observed, both clinically and experimentally, in the various effects of the two drugs. There is now considerable agreement that the use of epinephrine can induce disturbances of cardiac rhythm including ventricular fibrillation, especially in organically diseased hearts. On the other hand, with regard to norepinephrine, the situation is quite controversial. Von Euler[3] maintains that norepinephrine has a lesser tendency to produce arrhythmias than epinephrine. Nathanson and Miller[4] have shown that noradrenaline does not stimulate impulse-forming foci in the heart and does not encourage change of rhythm. Similarly, Sampson and Zipser,[5] Griffith et al.,[6] Binder et al.,[7] Smith and Guz,[8] and Miller et al.,[9] in reporting their observations on the use of noradrenaline in shock from myocardial infarction, do not mention any arrhythmias. On the contrary, Brooks et al.,[10] find the irritative effects on the myocardium to be the same with both amines.

While it is difficult to evaluate with precision the extent to which the use of noradrenaline can prove life-saving in cardiogenic shock, the present clinical tendency is certainly to use noradrenaline in this situation, the general impression being that it has no direct effect on the myocardium. However, Littler and McKendrick[11] studied the effects of L-noradrenaline on the myocardium in laboratory animals (dogs and monkeys) and in patients with myocardial infarction with shock. They found this amine capable of producing serious cardiac arrhythmias. This view is also substantiated by Maegraith[12] who believes that these arrhythmias can be prevented by simultaneous use of atropine. It has also been reported recently[13] that this drug is of great benefit in abolishing paroxysmal tachycardias. The effects of epinephrine and norepinephrine upon the electrocardiogram in

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experimental atherosclerosis have, however, not been studied. These contradictory data make it highly desirable to evaluate further the effects of these amines on cardiovascular dynamics under various conditions.

Methods

Young male white rabbits, weighing between 0.9 and 1.6 kg. were used. Three such groups of twelve animals each were employed. In each group six animals were maintained on a diet of Purina Chow Checkers alone and the remaining six on the same basic diet to which was added cholesterol (2 per cent) and corn oil (6 per cent). The animals were kept in individual cages, and the daily allotted food ration was 150 gm. with water *ad lib.* At weekly intervals each animal was weighed and the electrocardiogram (lead II) recorded with a Sanborn Visocardiette using the following procedure: the unanesthetized rabbit was placed in a wooden box, approximately 16 inches long by 6 inches wide by 6 inches deep. The box was just large enough to accommodate the body of the animal comfortably. The head of the animal projected through an opening in the front end of the box, and was free to move and readily accessible for making injections into the ear vein, after the lid of the box was closed. Hypodermic needles (22 gauge) were used as subcutaneous limb electrodes, the lead wires passing through suitable openings in the sides of the box. The animals soon became "conditioned" to the whole procedure and the initial electrocardiograms were taken only after five to ten minutes in the box.

At various intervals during periods ranging from four to thirty-eight weeks, intravenous test injections of epinephrine or norepinephrine in doses ranging from 10 μg. to 1 mg. were made into the marginal ear veins in corresponding "control" and "fat-fed" animals of each group. In all experiments the injections were made while the records were being taken and the recordings continued for one to two minutes thereafter. However, the electrocardiogram was continuously under observation and in most experiments records were taken until return to the normal pattern was observed (five to ten minutes in some instances). Freshly prepared solutions of L-epinephrine bitartrate* and L-norepinephrine bitartrate,* referred to throughout as "epinephrine" and "norepinephrine," were employed.

In the course of some of the experiments total blood cholesterol levels were determined in corresponding control and fat-fed animals, employing the Pelkan and Allen modification of the Bloor method. Finally, at the termination of the observation period (thirty-eight weeks) all surviving animals in both groups were killed, and in some cases the heart was immediately excised and perfused by a modified Langendorff method, recording simultaneously changes in coronary inflow and heart contractions, as previously described by Lu and Melville.[14] Sections of the heart were also examined microscopically in the remaining animals.

* Kindly supplied by the Winthrop-Sterling Research Institute, Rensselaer, New York.

Results

In regard to the electrocardiographic changes which were observed in the animals during the period of high fat-cholesterol feeding (without superimposed epinephrine or norepinephrine), the findings were entirely negative. In none of these animals was any significant deviation from the normal pattern detectable when the records of the control and high fat-fed animals were compared at corresponding periods even as long as thirty-eight weeks, in spite of the marked atherosclerotic changes which could be detected at autopsy in these animals. Some examples of the relatively normal appearance of the electrocardiograms taken prior to injections of either epinephrine or norepinephrine can be seen in the sections of the records marked control in the various figures herein.

It was observed that the responses to epinephrine and norepinephrine differed depending both on the duration of the high fat feeding and the dosage of the amines employed. The findings may be conveniently divided into (1) responses during the early period (four to twelve weeks), and (2) responses during the late period (nineteen to thirty-eight weeks). The changes which were recorded during the intermediate periods were more variable from animal to animal, and need no detailed consideration.

Early period (four to twelve weeks)

Following small doses (10 μg.) of either epinephrine or norepinephrine, no significant differences could be detected in the responses of the control and the fat-fed groups of animals. In both groups (forty-two observations) there was only a slight transient bradycardia or tachycardia, but no abnormal ST-T changes or arrhythmias recorded in either the control or the fat-fed animals. However, following injections of high doses of either agent, definite electrocardiographic changes occurred in both groups. Some examples of these changes are shown in Figures 1 and 2.

As can be seen from Figure 1, injection of 0.1 mg./kg. of norepinephrine in the control animal led to a sustained bradycardia, but no significant change in the ST-T segment. While, following a similar injection in the fat-fed animal, there

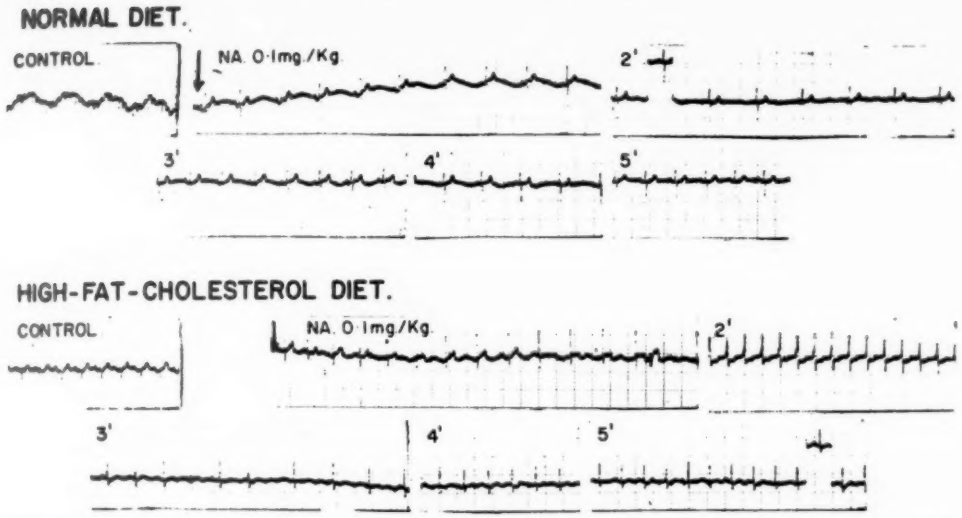

FIG. 1. Electrocardiographic records showing comparative effects of norepinephrine (NA—0.1 mg./kg.), fourth week of experimentation. See text.

was a brief initial bradycardia, followed by tachycardia, before restoration to the control rate. These changes were also associated with definite ST depression and negative T waves.

In Figure 2, it can be seen that following injection of 0.1 mg./kg. of epinephrine in the control animal, again there was a marked and sustained bradycardia, associated with heart block and ventricular arrhythmias. However, there were no definite ST-T changes detectable. On the other hand, following similar injection of epinephrine in the fat-fed animal, the initial bradycardia was followed by normal beats and paroxysmal tachycardia (300 per minute) with corresponding ST-T changes (sagging ST and diphasic T waves). In this experiment restoration to normal rhythm (although at a slower rate) also occurred in about four minutes.

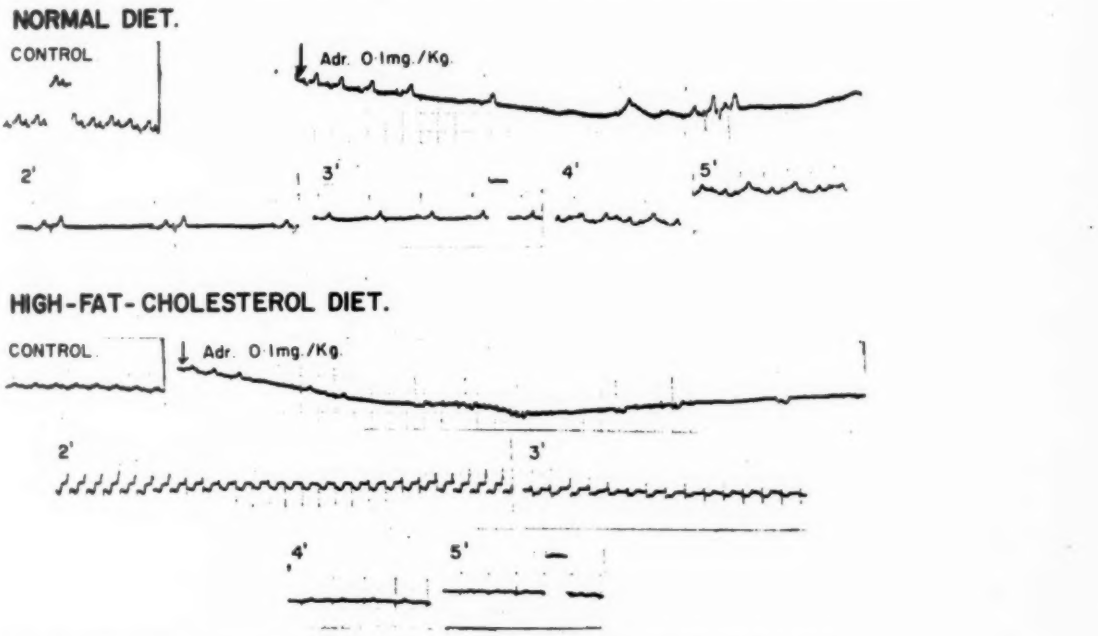

FIG. 2. Electrocardiographic records showing comparative effects of epinephrine (Adr—0.1 mg./kg.), fourth week of experimentation. See text.

TABLE I

Typical Electrocardiographic Changes Following Injection of Adrenaline or Noradrenaline in Rabbits with Normal or High Fat-Cholesterol Diets (Nineteen to Thirty-eight Weeks of Experimentation)

Rabbit No.	Dose (μg.)		Rate	Irregularities of Rhythm*	ST-T	Remarks
	Untreated Control Group	High Fat-Cholesterol Group				
			Adrenaline (22 Obs.)			
15	100		<	+++	No change	Auricular fibrillation
4		100	<	++++	No change	Ventricular fibrillation
1	200		<	++++	No change	Ventricular fibrillation
6		200	<	++++	No change	Ventricular fibrillation
15	500		<	++++	No change	Ventricular fibrillation
16		500	<	++++	Inverted T	Ventricular fibrillation
			Noradrenaline (17 Obs.)			
3	100		<	—	Sagging ST	
17		100	<	+++	Sagging ST	Auricular tachycardia with aberrant conduction
3	200		<	—	Sagging ST	Periods of A-V block
5		200	<	+++	No change	Short runs of paroxysmal tachycardia
13	500		<	+++	No change	Runs of paroxysmal tachycardia
17		500		+++	No change	Tachycardia with aberrant conduction
3	1,000		<	+++	Sagging ST	Auricular paroxysmal tachycardia
6		1,000	<	+++	Inverted T	Auricular paroxysmal tachycardia

* Occasional ectopic beats (+); frequent ectopic beats (++); tachycardia of various types (+++); ventricular fibrillation (++++).

Findings, similar to those described, have been observed in three different animals in each type of experiment illustrated. It would, therefore, appear that even in this early period of fat-feeding injections of high doses of epinephrine or norepinephrine induce more marked electrocardiographic changes than in rabbits kept on a normal diet. However, while ventricular arrhythmias were seldom seen with norepinephrine, this agent induced definite ST-T changes in the fat-fed animals, which were not observed in the normal animals.

It is also of interest to note that at the end of the twelve-week period of cholesterol-high fat feeding in this group of experiments, the blood cholesterol levels in two of the animals were 269 and 405 mg. per cent, in comparison with 58 and 66 mg. per cent in two of the control animals. Postmortem examination of the hearts of the fat-fed animals, even at this early stage, showed characteristic gross atherosclerotic changes.

LATE PERIOD (NINETEEN TO THIRTY-EIGHT WEEKS)

In view of these intense effects associated with intravenous injections of high doses of the amine even in normal animals, it was felt that after animals were maintained on high cholesterol diets for long periods, it might be possible to elicit similar changes with smaller doses of the amines. However, again even after nineteen to thirty-eight weeks of fat feeding, no significant electrocardiographic alterations could be induced in either the control or fat-fed animals following injections of 10 μg. doses of either epinephrine or norepinephrine. With doses exceeding 100 μg. (irrespective of body weight) it was nevertheless possible to detect rather striking changes.

Effects of Epinephrine and Norepinephrine: In Table I, are summarized data obtained from both untreated control and cholesterol-high-fat groups of animals following injections of test doses of epinephrine (100 to 500 μg.) and norepinephrine (100 to 1,000 μg.). Some typical illustrations of the electrocardiographic records obtained in some of these experiments are shown in Figures 3 to 5.

As can be seen, in all animals (both control and fat-fed) receiving injections of epinephrine,

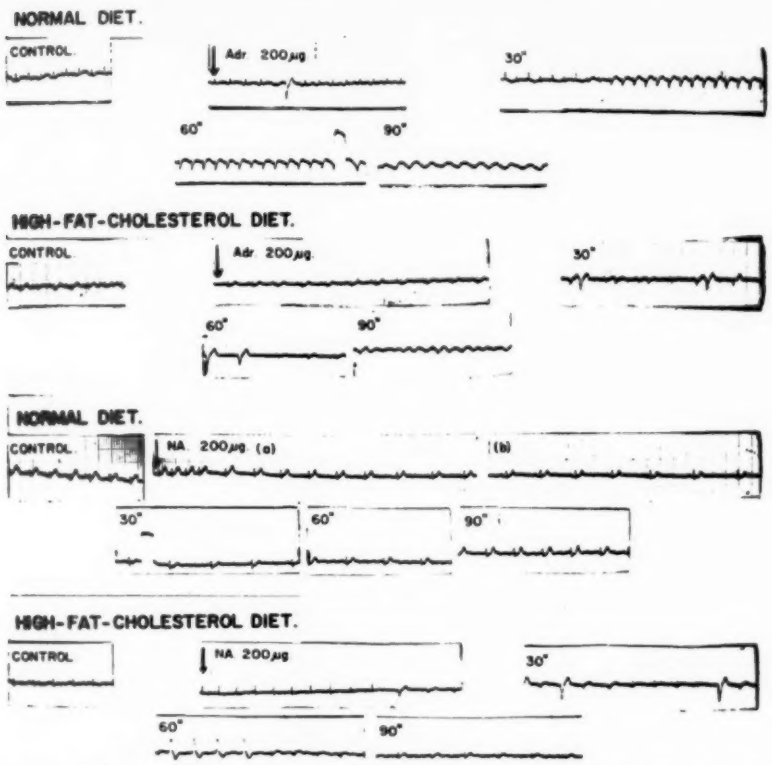

FIG. 3. Electrocardiographic records showing comparative effects of epinephrine (Adr.—200 μg.), thirty-sixth week of experimentation; and norepinephrine (NA—200 μg.) thirty-second week of experimentation. See text.

there was a slowing of heart rate associated with various arrhythmias—frequent ectopic beats, paroxysmal tachycardia, and auricular and ventricular fibrillation. There were, however, no significant detectable ST or T wave changes in most of these experiments.

The table also shows that following injections of norepinephrine, in doses of 100 to 200 μg. in the untreated control animals, there were no ventricular arrhythmias, but only a bradycardia with A-V block and temporary sagging of the ST segment. Similar doses of norepinephrine induced, in addition to these changes, paroxysmal tachycardia in the fat-fed animals. Increasing the doses of norepinephrine to 500 and 1,000 μg. led to rather similar changes in both groups of animals. Despite these high doses of norepinephrine, there was no evidence of ventricular fibrillation in these animals, and return to normal sinus rhythm ensued in all cases.

It is therefore clear that both in the control and fat-fed animals, epinephrine induces more intense arrhythmias than norepinephrine. However, in the norepinephrine group there appears to be more striking ST-T changes than in the epinephrine group, but the rapid development of tachycardia in the latter experiments might have obscured these changes. It is nevertheless clear that fatal ventricular fibrillation occurs only with epinephrine under these conditions.

Blood Cholesterol Levels: In regard to the blood cholesterol levels observed in this group, it was found that after nineteen weeks of the high fat administration, total cholesterol levels of 880 and 1,440 mg. per cent were observed in two animals, in contrast to values of 83 and 85 mg. per cent in two control animals. After thirty-four weeks of cholesterol-high fat feeding, three animals showed concentrations of 1,032, 1,460 and 1,910 mg. per cent, respectively, while two control animals showed concentrations of 88 and 77 mg. per cent. It is therefore obvious that all these fat-fed animals were in a sustained and advanced state of hypercholesteremia throughout this later period of observation. Moreover, postmortem histologic examinations of the heart and aorta of all animals showed marked atherosclerotic involvement. A typical

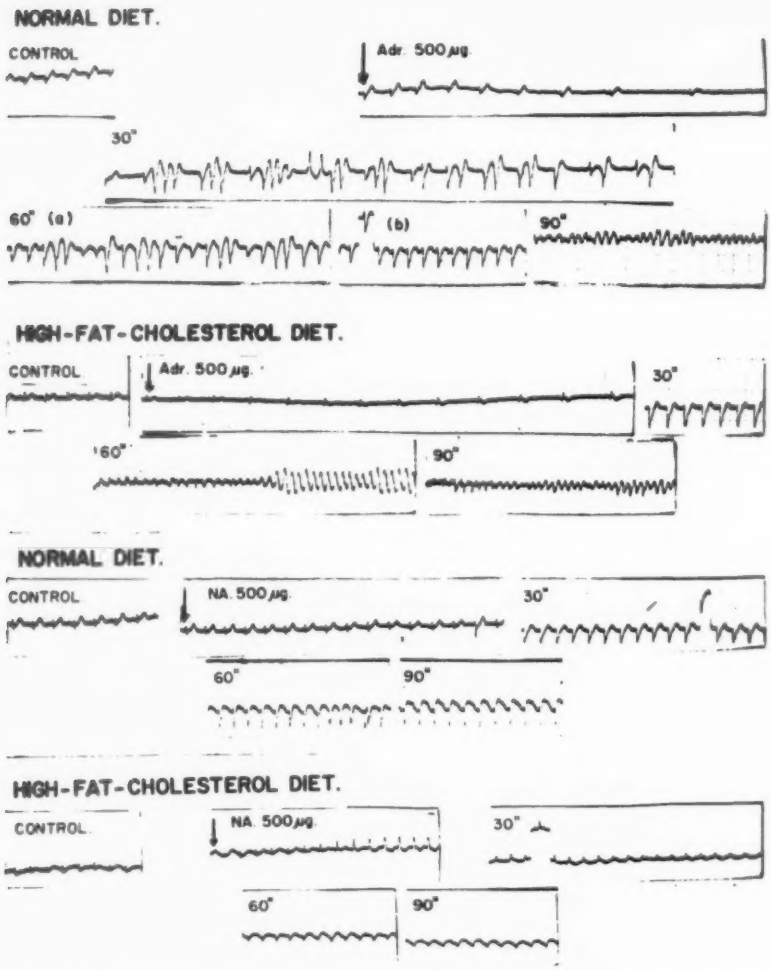

FIG. 4. Electrocardiographic records showing comparative effects of epinephrine (Adr.—500 µg.), twentieth and twenty-eighth week of experimentation, respectively; and below, norepinephrine (NA—500 µg.), twenty-first and thirtieth week of experimentation, respectively. See text.

illustration of these changes in the coronary vascular tree is shown in Figure 6.

Coronary Flow and Myocardial Contractility: Finally, Figure 7 shows comparatively the changes in the coronary flow and heart contractions as recorded from excised hearts from control and cholesterol-high fat-fed animals. In a general way, the rates of coronary flow were somewhat higher in the latter group, but the amplitude of the contractions was also less. Following injection of either epinephrine or norepinephrine in the normal heart preparation (Figure 7, upper record), the usual marked increased contractility of the myocardium associated with gradually increasing coronary flow can be seen. On the other hand, following similar injections of the amines in the fat-fed groups (Figure 7, lower records) there was only a slight immediate cardiac stimulation with little associated change in coronary flow. In the noradrenaline experiment in this group the coronary rate before the injection was higher than is usually observed, and following the injection there was diminution of the coronary flow with improved cardiac contractility. These findings would suggest that with the establishment of atherosclerosis there is diminished myocardial contractility and a corresponding lack of the usual coronary dilatation following injections of the amines.

COMMENTS

Electrocardiogram at Rest: The findings presented show that even with the development of

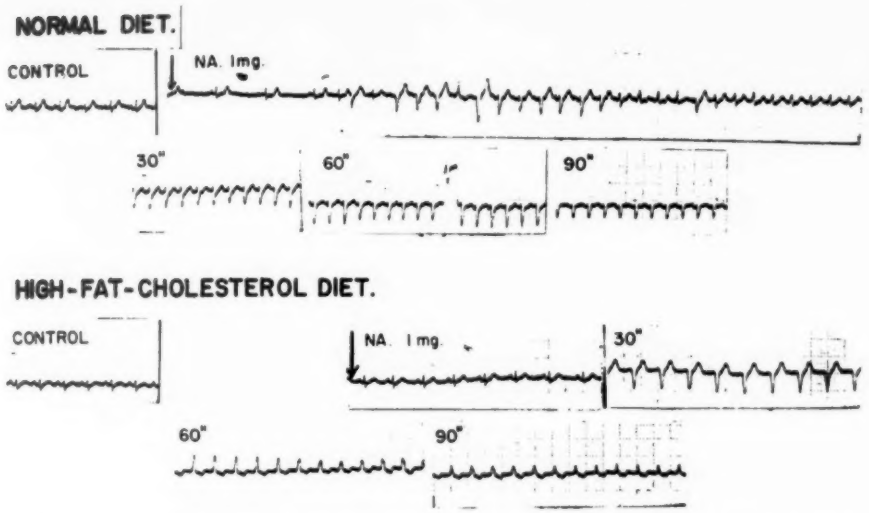

FIG. 5. Electrocardiographic records showing effects of norepinephrine (NA—1 mg.), thirty-eighth week of experimentation. See text.

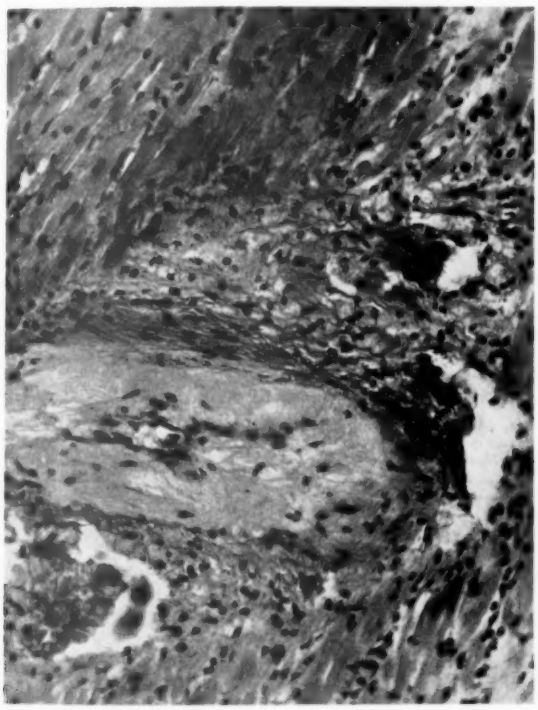

FIG. 6. A small coronary artery showing heavy subintimal accumulation of foamy histiocytes with marked stenosis of its lumen, some adventitial deposits of similar but smaller histiocytes and patchy disappearance of its muscularis. Hematoxylin and eosin × 200.

advanced coronary atherosclerotic changes, induced by a high cholesterol-high fat diet, no spontaneous characteristic anoxic electrocardiographic changes (ST-T alterations) could be detected in these rabbits. This might conceivably be due to the slowly progressive development of the condition, with establishment of compensatory collateral channels to meet the oxygen demands of these animals, which were kept isolated and in confinement to relatively small cages. Whether or not these environmental conditions contributed to these somewhat anomalous results is not clear. However, our observations are in agreement with those of most workers, although Rinzler, Travell and Karp[15] have reported slight depression of the ST segment in some rabbits maintained on a similar high cholesterol-high fat diet for twenty to twenty-two weeks. Franco[16] has also reported distinct ST and T changes, which developed spontaneously in rabbits kept on a high fat-cholesterol diet. It is not clear from these latter reports whether the animals were kept in separate cages (relatively inactive) or together in a common cage. It is conceivable that rather different results might be observed if the animals are kept together in a more active state, and this question is now being investigated.

Electrocardiogram After Epinephrine and Norepinephrine: It is also evident that small intravenous doses (10 μg.) of either epinephrine or norepinephrine do not significantly influence the electrocardiogram in either control or fat-fed rabbits. On the other hand, with excessive doses of the amines (50 to 100 μg. per kg.), there was more marked tachycardia with either agent in the fat-fed group than in the control group, although ventricular arrhythmias clearly developed more

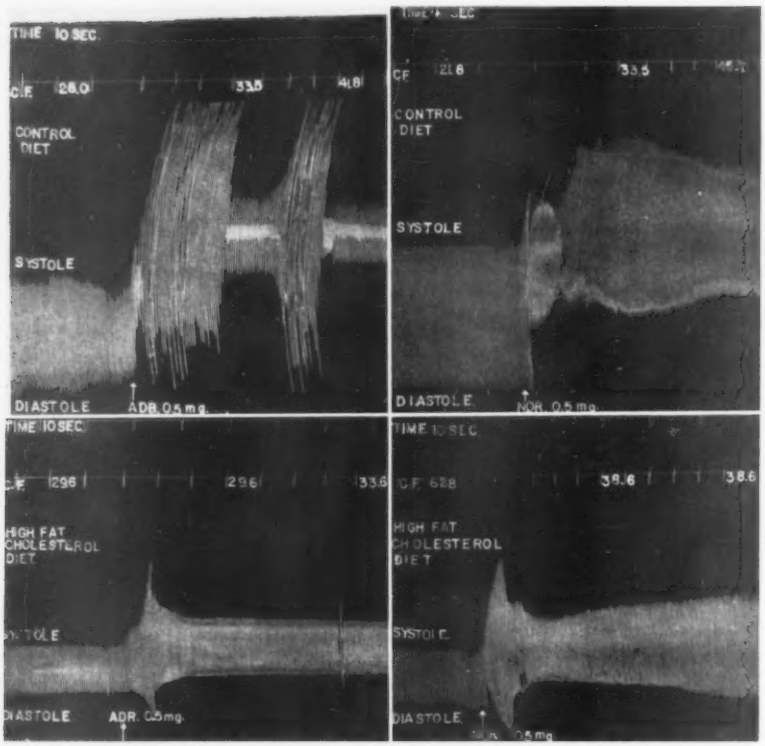

FIG. 7. Excised perfused rabbit hearts from normal and fat-fed groups, showing simultaneous coronary flow per minute (C.F.) and heart contraction changes, and the responses to epinephrine (Adr—0.5 mg.) and norepinephrine (NA—0.5 mg.).

frequently with epinephrine than with norepinephrine. In regard to the ST-T changes in these experiments, it is also of interest to note that these were more strikingly seen with noradrenaline in the high fat-cholesterol group than in the normal untreated groups. Indeed, after the administration of epinephrine in either group ST-T changes were surprisingly slight. However, as already pointed out this might be due to the more marked tachycardia induced by epinephrine.

Cardiac Arrhythmias: It is also apparent from these experiments that epinephrine leads to more striking arrhythmias than norepinephrine, and with high doses (100 to 500 μg.) transient or fatal ventricular fibrillation ensued in all animals (both control and high-fat fed). On the other hand, although more marked ST-T changes developed following the injection of norepinephrine, fatal ventricular fibrillation could not be precipitated in any of the animals tested with doses as high as 1 mg. These findings confirm the danger associated with the use of epinephrine as a test for coronary function, but would suggest that norepinephrine might be a satisfactory agent. It is now quite clear that in general norepinephrine exerts much less deleterious cardiac effects in man since it has been recently employed to counteract shock in patients following myocardial infarction. It would therefore appear that its use as a diagnostic test might be well worth exploring.

The exact mechanism of production of the arrhythmias described herein is still obscure. In view of the high doses of the amines required to obtain these changes, it is possible that both vagal and non-vagal effects might be involved. Littler and McKendrick[11] have observed that cardiac arrhythmias induced by the administration of epinephrine and norepinephrine in anesthetized dogs and monkeys can be prevented by previous atropinization. However, contrary to the relative safety of norepinephrine described herein, these authors conclude that "in view of the definite danger of producing serious cardiac arrhythmias with noradrenaline, we believe that if the drug is to be used at all it should only be used in myocardial infarction under direct electrocardiographic supervision." Maegraith[12] has also published some confirma-

tory results in anesthetized monkeys, and suggests that it might be worthwhile to employ atropine to minimize the risk of cardiac arrhythmias during the administration of norepinephrine in cardiac or any other form of shock. It might also be added that in a few preliminary experiments we have also observed that previous atropinization protects the unanesthetized rabbit against arrhythmias caused by both epinephrine and norepinephrine. This aspect of the problem, as well as the associated changes in blood pressure under similar experimental conditions to those employed in this study, are also being investigated.

Cardiac Contractility: Finally, in regard to the observations on the isolated perfused hearts, it would appear that contractility is rather lessened in the atherosclerotic hearts and the contractile responsiveness to both epinephrine and norepinephrine is diminished, although definite tachycardia still ensued. Under these conditions also the usual changes in coronary flow induced by the amines are not observed. It is possible that the reduced contractility of the myocardium might be a factor both in this latter phenomenon and also in preventing the expected deleterious cardiac effects of the amines in the presence of this type of experimental atherosclerosis. Indeed, in many experiments it appeared that apart from the more marked tachycardia, the electrocardiographic changes observed were often less striking in the atherosclerotic animal than in the normal animal. Although the exact significance of these findings is not clear, the fact that the sensitivity of the heart to epinephrine and norepinephrine is not greatly increased during the course of this type of experimental atherosclerosis, would rather suggest that release of adrenaline or noradrenaline in the body is not a major factor in precipitating sudden fatalities from coronary disease. The problem, however, requires further study.

Summary

1. It has been observed that rabbits maintained on a high fat-cholesterol diet for periods ranging up to thirty-eight weeks, show no significant anoxic electrocardiographic changes (STT alterations) as compared with normal rabbits.

2. Following injections of epinephrine in doses ranging from 100 to 500 μg. marked ventricular arrhythmias and even fatal ventricular fibrillation ensue in both normal and high fat-fed animals, although no significant ST-T changes were detectable.

3. Following the injection of norepinephrine in doses of 100 and 200 μg., tachycardias of various types ensued only in fat-fed animals, but with higher doses (500 and 1,000 μg.) similar changes occurred in both normal and fat-fed animals.

4. Norepinephrine under these conditions induces rather characteristic anoxic ST-T changes, but no ventricular fibrillation.

5. Perfused isolated atherosclerotic hearts show diminished contractility and reduced responses to epinephrine and norepinephrine.

6. It is concluded, therefore, that norepinephrine is less injurious than epinephrine to both the normal and the atherosclerotic heart.

Acknowledgment

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References

1. Levine, S. A., Ernstene, H. C. and Jacobson, B. M. The use of epinephrine as a diagnostic test for angina pectoris. *Arch. Int. Med.*, 45: 191, 1930.
2. Katz, L. N., Hamburger, W. W., and Lev, M. Diagnostic value of epinephrine in angina pectoris. *Am. Heart J.*, 7: 371, 1932.
3. Von Euler, U. S. Noradrenaline in hypotensive states and shock. *Lancet*, 2: 151, 1955.
4. Nathanson, M. H. and Miller, H. The action of norepinephrine, epinephrine, isopropyl norepinephrine on the rhythmic function of the heart. *Circulation*, 6: 238, 1952.
5. Sampson, J. J. and Zipser, A. Norepinephrine in shock following myocardial infarction. *Circulation*, 9: 38, 1954.
6. Griffith, G. C., Wallace, W. B., Cochran, B., Jr., Nerlich, W. E. and Frasher, W. G. The treatment of shock associated with myocardial infarction. *Circulation*, 9: 527, 1954.
7. Binder, M. J., Ryan, J. A., Jr., Marcus, S., Mugler, F., Jr., Strange, D. and Agress, C. M. Evaluation of therapy in shock following acute myocardial infarction. *Am. J. Med.*, 18: 622, 1955.
8. Smith, S. K. and Guz, A. L-noradrenaline in treatment of shock in cardiac infarction. *Brit. M. J.*, 2: 1341, 1953.
9. Miller, A. J., Cheng, T. O. and Freedman, M. E. Electrocardiographic changes during norepinephrine-induced hypertension in normal man. *Am. Heart J.*, 50: 567, 1955.
10. Brooks, C. M., Hoffman, B. F., Suckling, E. E. and Orias, O. Excitability of the Heart, p. 219. New York, 1955. Grune & Stratton.
11. Littler, T. R. and McKendrick, C. S. L-noradrenaline in myocardial infarction. *Lancet*, 2: 825, 1957.
12. Maegraith, B. G. Noradrenaline in shock. *Lancet*, 2: 891, 1957.
13. McGin, J. T. and Schluger, J. Levarterenol bi-

tartrate (Levophed) in the treatment of cardiac arrhythmias. *Am. Heart J.*, 50: 625, 1955.

14. Lu, F. C. and Melville, K. I. A new apparatus and procedure for continuous registration of changes in coronary flow concurrently with changes in heart contractions. *J. Pharmacol. & Exper. Therap.*, 99: 3, 1950.
15. Rinzler, S. H., Travell, J. and Karp, D. Detection of coronary atherosclerosis in the living animal by the ergonovine stress test. *Science*, 121: 900, 1955.
16. Franco, A.: Electrocardiography in experimental artherosclerosis and hypertension. *Am. Heart J.*, 54: 69, 1957.

Case Report

Congenital Pulmonary Artery Atresia with Associated Tricuspid Hypoplasia

Report of Two Cases*

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Since the advent of cardiac catheterization, angiocardiography and the feasibility of surgical correction or palliation of the malformed heart, the medical literature has been replete with reports of diagnostic, physiologic and anatomic studies on congenital heart disease. These reports run the gamut of recording studies on the simplest to the most complex of congenital heart deformities. Yet a search of the literature reveals scant references to congenital pulmonary artery atresia with tricuspid hypoplasia.[1–3] Our purpose is to report two such cases with our observations.

Case Reports

Case 1. The patient was a baby boy (00-17-81), nine days old, who was born on February 6, 1956, full term, weighing 8 pounds, 8 ounces; he was cyanotic at birth. At thirty-six hours of age, a grade 2 systolic murmur was heard at the second to third intercostal spaces. At four days of age, blood studies revealed a hemoglobin of 17 gm. per cent, 5,500,000 red blood cells per cu. mm., and a hematocrit of 56 per cent. An electrocardiogram taken on the second day of life revealed a regular sinus rhythm, P-R interval of 0.16 second, extreme right axis deviation (−100 degrees), peaked P waves, and RSr pattern in all the precordial leads V_1 through V_5.

Roentgenologic and Electrocardiographic Findings: A posteroanterior chest x-ray was reported as showing a coeur-en-sabot configuration of the heart with exceptionally clear lung fields. After a week's observation, cyanosis was noted to be increasing. In view of this, an angiocardiogram was performed.

Significant angiocardiograms (Fig. 1) revealed the following salient features: Simultaneous opacification of both right and left atria, followed by opacification of the left ventricle, aorta and pulmonary arteries in that order without demonstration of the right ventricle at any time. In spite of the extreme right axis deviation noted in the electrocardiogram, the opinion was that the angiocardiograms were compatible with tricuspid atresia.

The electrocardiogram taken on the third day of life (Fig. 2) was identical to the one taken on the second day of life except that the right precordial leads were also recorded.

Autopsy Findings: On the ninth day of life, the baby died. Autopsy was limited to the thorax. A description of the heart was as follows: The venous return to the right auricle was normal. Both atria were enlarged and a large defect in the atrial septum was demonstrated. The mitral valve was normal except for slight roughening of the edges of the valve leaflets. The left ventricle was enlarged and hypertrophied. The aortic root was normal and the arch was moderately enlarged. A moderate-sized patent ductus existed, supplying the only flow of blood through hypoplastic pulmonary arteries. Pulmonary atresia was present without a vestige of any proximal artery. The right ventricle was extremely thick walled and the cavity was only potential. The interventricular septum was intact. The tricuspid valves were formed but diminutive and with roughened edges. The effective orifice measured only 2 mm. in diameter. The tricuspid ring was markedly constricted, measuring 1 cm. in diameter.

Case 2. The patient was a baby girl (07-00-52), thirteen months of age, weighing 12 pounds and 12 ounces. At birth on January 23, 1957, cyanosis was noted. On the following day, persistence of the cyanosis and a loud "precordial" systolic murmur were noted. Blood data revealed 13.2 gm. per cent

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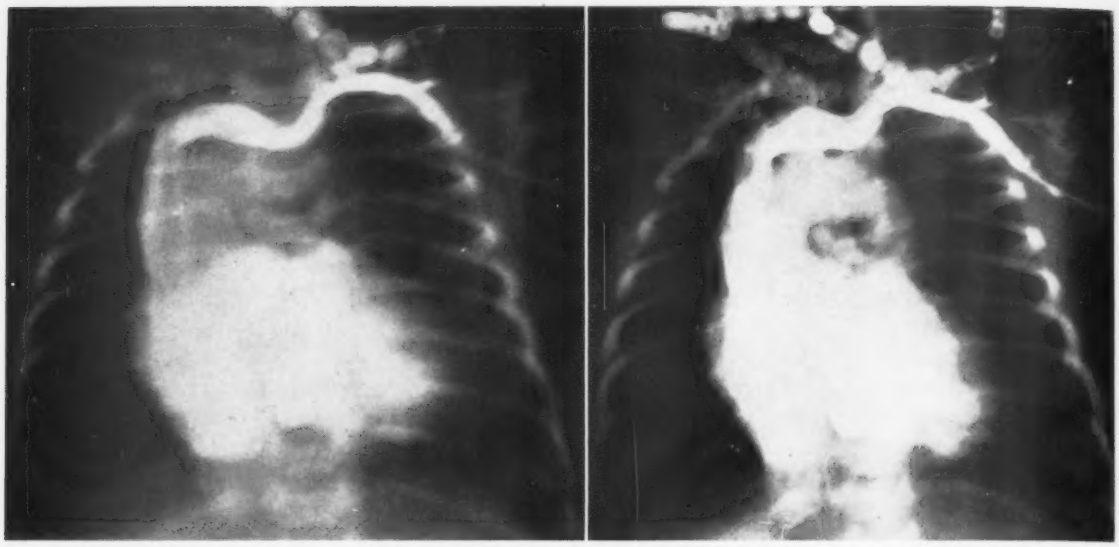

FIG. 1. *Left*, opacification of right and left atria. *Right*, opacification of left ventricle, aorta and pulmonary arteries.

hemoglobin, 3,800,000 red blood cells per cu. mm., and 38 per cent hematocrit. On January 31, 1957, cyanosis of the lips and nailbeds became moderate to severe on crying. The only significant finding was a loud blowing systolic murmur heard best over the third to fourth left parasternal interspaces.

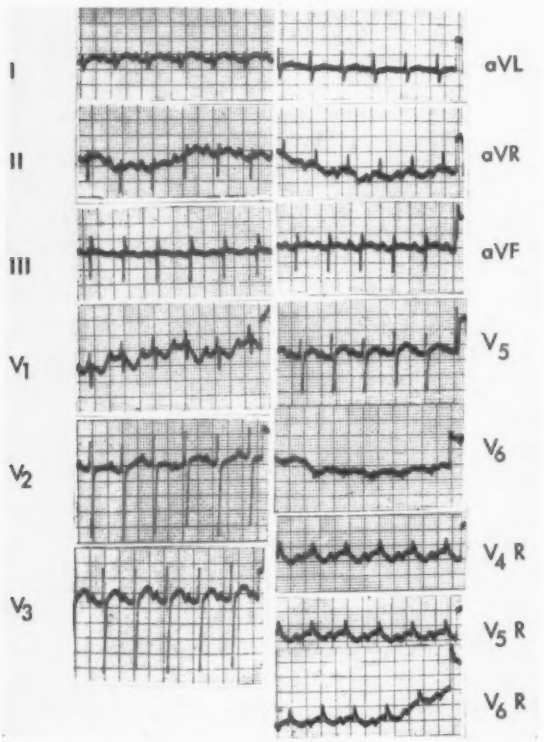

FIG. 2. Extreme right axis deviation, peaked P waves, RSr pattern in precordial leads V_1 to V_5, qR pattern in right precordial leads.

A posteroanterior roentgenogram of the chest was reported as showing no definite abnormality of the heart. An electrocardiogram taken two days after birth revealed an axis deviation of +65 degrees, with normal precordial and unipolar leads for an infant of this age. On the basis of these data, a diagnosis of cyanotic congenital heart disease with right-to-left shunt was made. Monthly observations were suggested, and a recommendation for angiocardiographic studies if cyanosis intensified at rest. On February 1, 1957, the infant was discharged from the hospital. Her weight was 5 pounds, 14 ounces.

On January 18, 1958, readmission to the hospital was occasioned by an upper respiratory infection. The essential findings at this time were temperature 102.5°F., generalized cyanosis, red injected pharynx, respiratory rate of 60 per minute and heart rate of 160 beats per minute. No murmur was audible at this time. Laboratory data revealed a hemoglobin of 19.8 gm., white count of 9,800 cells per cu. mm., with a differential of 59 per cent segmented cells, 20 per cent stab cells, 13 per cent lymphocytes and 8 per cent monocytes, and a hematocrit of 80 per cent. A throat culture revealed a pure growth of gamma streptococci. Under intensive antibiotic therapy, improvement ensued and the throat culture became negative. At this time cyanosis was less intense.

Roentgenographic and Electrocardiographic Findings: On February 14, 1958, angiocardiography under general anaesthesia was carried out with simultaneous lateral and anteroposterior views (Fig. 3). The flow of contrast material went from right to left atria, thence to left ventricle, aorta and, in $^1/_6$ second, to hypoplastic pulmonary arteries. The right ventricle was never visualized.

An electrocardiogram (Fig. 4) taken at twelve months of age revealed a regular sinus tachycardia at 160 beats per minute; P-R interval of 0.12 second

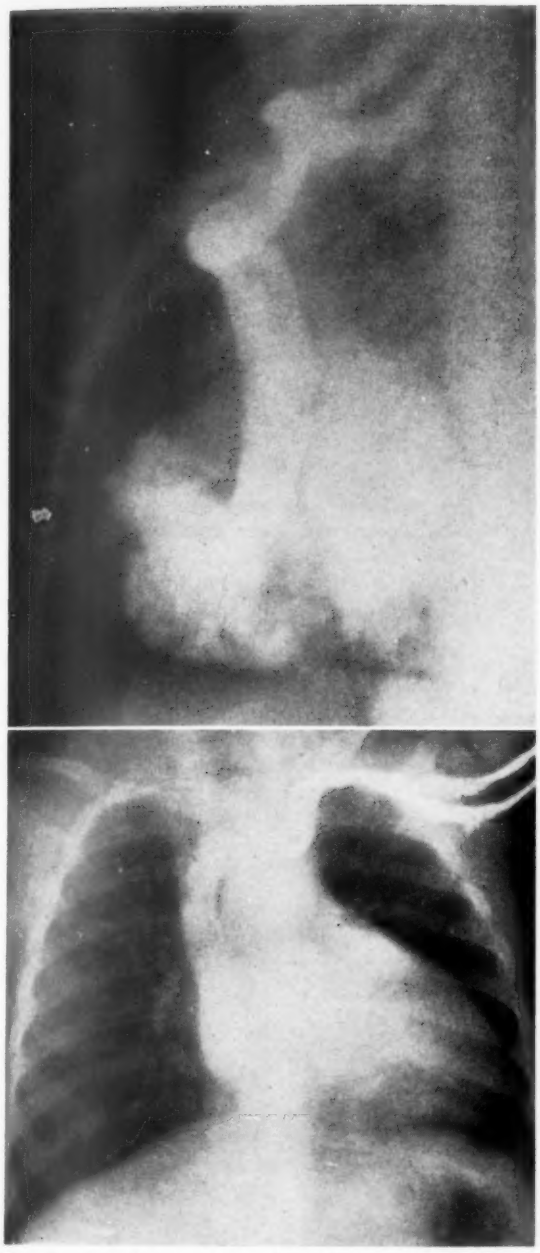

FIG. 3. Simultaneous lateral and anteroposterior views reveal flow of contrast material from right to left atrium, thence to left ventricle and aorta.

QRS of 0.06 second; tall peaked P waves in lead II and notched and deformed in V_3 through V_6; inverted T waves in leads II and III, rS pattern V_1 to V_6 and aVL. Right axis deviation (+110 degrees) was present.

The decision was then made to perform a Potts procedure under hypothermia. Cardiac arrest occurred after opening of the chest and effective resuscitation could not be accomplished.

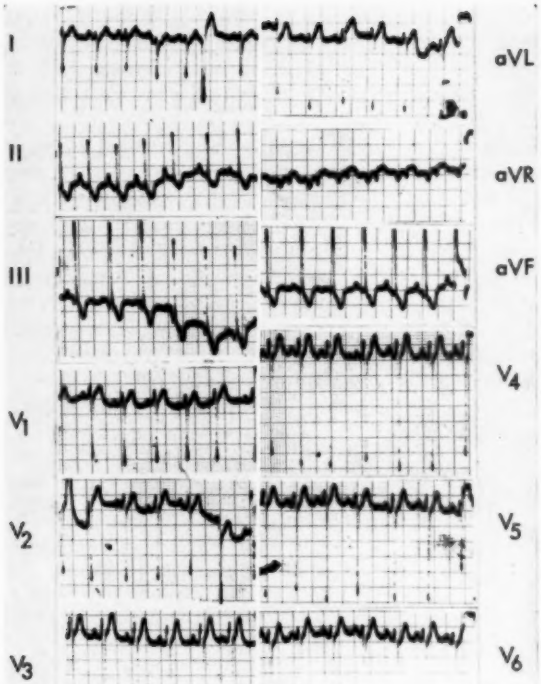

FIG. 4. Peaked P waves in lead II and notched in V_3 to V_6; inverted T waves leads II and III, rS pattern V_1 to V_6 and aVL.

Autopsy Findings: Autopsy was performed.* The only anomaly found was cardiac. A description of the heart and great vessels follows: The heart showed a definite hypertrophy, particularly in its transverse diameter. On external examination, the right ventricular wall was greatly thickened and formed a rather firm mass about the size of a walnut. The aorta was in its normal position and was quite wide, measuring 1.7 cm. in diameter. In contradistinction, the pulmonary artery trunk was greatly reduced in size and measured only 7 mm. in transverse diameter. The right atrium was then opened and found to be normal except for the presence of an oval-shaped defect communicating with the opposite atrium. This formed a semilunar longitudinal slit measuring 1.5 cm. in length, and this area could be readily distended by the fingertip. The tricuspid ring was markedly stenotic and measured 7 mm. in diameter, while the tricuspid valve opening measured only 3 mm. The leaflets were small and greatly hypoplastic. The outside length of the right ventricle was 4.3 cm. and the wall of the right ventricular was tremendously thickened and measured 1.5 cm. The cavity of the right ventricle was greatly reduced in

* Autopsy performed and described by Louis R. Ferraro, M.D., Director of Pathology Department, Nassau Hospital, Mineola, New York.

size and extended only 1.3 cm. below the tricuspid ring. There was no communication from the ventricular cavity on this side of the pulmonary trunk. There was no evidence of any interventricular septal defect.

The left atrium was essentially normal as were the mitral valve and ring. The left ventricular wall did not show any significant gross changes or congenital anomalies. The aortic ring and leaflets appeared normal. A persistent ductus arteriosus was present which was 9 mm. in length and had a diameter of 4 mm. The pulmonary artery and trunk were then closely examined. There was a complete atresia of the pulmonary trunk with no evidence whatsoever of any valvular formation. Two small dimples were present at the site of what should have been the valve.

Comments

The type of congenital cardiac lesion reported here is rare but it may be more common than previously suspected. This lesion would be most easily confused with tricuspid atresia Type 1A.[4] Both conditions evidence cyanosis from birth and may be radiologically and angiographically indistinguishable. However, congenital pulmonary artery atresia with associated tricuspid hypoplasia characteristically reveals a right axis deviation in the electrocardiogram in contrast to the more characteristic left axis deviation evidenced by tricuspid atresia. There is only one proved case of the latter, by autopsy findings, that demonstrated electrocardiographic right axis deviation.[5]

Other authors[6,7] have made mention of having clinically observed tricuspid atresia with right axis deviation. In these latter instances it may well be that the type of congenital deformity described in our cases may be present rather than tricuspid atresia. Other cases have been diagnosed as "non-functioning right ventricle,"[3] or "isolated pulmonary atresia."[8] Indeed, cases of true isolated pulmonary atresia are very rare and we believe this diagnosis should be reserved for those with normal tricuspid valves.

References

1. Edwards, J. E. In: Pathology of the Heart. Edited by Gould, S. E. Chap. 5, Springfield, Ill., 1953. Charles C Thomas.
2. Edwards, J. E., Dry, J. J., Parker, R. L., Burchell, H. B., Wood, E. H. and Bulbulian, A. H. An Atlas of Congenital Anomalies of the Heart and Great Vessels. Springfield, Ill., 1954. Charles C Thomas.
3. Taussig, H. Congenital Malformations of the Heart. New York, 1947. The Commonwealth Fund.
4. Edwards, J. E. and Burchell, H. B. Congenital tricuspid atresia; classification. *M. Clin. North America*, 33: 1177, 1949.
5. Sullivan, J. J., Jr. and Mangiardi, J. L. Tricuspid atresia with right axis deviation. Case report and review. *Am. Heart J.*, 55: 450, 1958.
6. Nadas, A. S. Pediatric Cardiology. Philadelphia, 1957. W. B. Saunders Co.
7. Brink, A. J. and Neil, C. A. The electrocardiogram in congenital heart disease. *Circulation*, 12: 604, 1955.
8. Glaboff, J. J., Gohmann, J. T. and Little, J. A. Atresia of the pulmonary artery with intact system. *J. Pediat.*, 37: 396, 1950.

Historical Milestones

Claude Bernard on Cardiac Catheterization

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Buenos Aires, Argentina

FEW MEN have attained such long-lasting success in their scientific endeavors as has Claude Bernard. Fighting against hostile surroundings, which included the lack of encouragement and actual resistance from his wife, conducting research in a cold and unhealthy room which could hardly be called a laboratory by present day standards, he not only made relevant discoveries in astonishing succession, but also laid the basis of modern experimental medicine.

In effect, although many distinguished investigators preceded Bernard in biologic research, such as Harvey, John Hunter, Spallanzani, Haller and Magendie, his own master, Bernard was the first to establish the experimental method as it is conducted today, in his book "Introduction à L'étude de la Médicine Expérimentale," the efficiency of which was proved by the extensiveness and quality of his discoveries. Speaking of Dandy's work on hydrocephalus, Halsted is supposed to have said[1] ". . . Few men make more than one great contribution to medicine." Perhaps Bernard, the physiologist, is the obvious exception to this rule.

His original work can be summarized as follows:[2] action of pancreatic secretion on fat absorption; glucogenic function of the liver; the role of vasomotor nerves; the foundation of scientific toxicology, with studies on curare and carbon monoxide intoxication; and investigation on animal heat production. His theoretical concepts of internal secretions and the idea of organic unity, are no less important. For these epoch-making contributions, Bernard is known world-wide. Perhaps less knowledge is available on the means he employed to these ends, i.e., his systematic and established operative method of research, published after his death in a volume entitled "Physiologie Opératoire"[3] (Fig. 1).

Although cardiac catheterization in the experimental animal had already been performed by Cheveau and Marey in the horse, Bernard used it as a routine procedure in his laboratory, and it is clearly and masterly described in his book (Fig. 2). Today, cardiac catheterization is widely employed as a diagnostic and research tool in cardiovascular disease. It is well to remember those pioneers who, by their work in the experimental laboratory, made possible its use by Forssmann; Padilla, Cossio and Berconsky; Jimenez Díaz and Cuenca; and its further development and clinical application by Cournand and Richards, Dexter, Bing, Soulié, Lenègre, Limón and many others. A translation of the pertinent paragraphs is here offered.[3]

* * *

BERNARD ON CARDIAC CATHETERIZATION

. . .But the most interesting point to us is the study of the heart by means of catheterization, that is to say, by the introduction of catheters in the great vessels that we advance until they get into the heart. Everybody knows the beautiful experiences by which Cheveau and Marey, introducing catheters into the atria and ventricles, could determine the pressures that develop in these cavities as they contract, and establish with certainty the synchronism of their contractions.

. . .To get into the heart we have several routes, and we can arrive at the right and the left chambers. It is quite easy to arrive at the right heart (Fig. 3). To this effect, we introduce a catheter in the jugular vein, entering directly into the heart, as the superior vena cava has no valve. Moreover, the valve of the inferior vena cava is not a serious obstacle, and advancing the catheter a little bit more, we can get it into this vein.

. . .It is more difficult to get into the left heart. We choose, to this effect, the carotid artery, sliding through it up to the origin of the aorta. Here, however, we find the aortic valves that are never com-

COURS DE MEDECINE

DU COLLÉGE DE FRANCE

LEÇONS

DE

PHYSIOLOGIE OPÉRATOIRE

PAR

CLAUDE BERNARD

Membre de l'Institut (Académie des sciences et Académie française), Professeur au Collége de France et au Muséum d'histoire naturelle.

AVEC 116 FIGURES INTERCALÉES DANS LE TEXTE

PARIS

LIBRAIRIE J.-B. BAILLIÈRE ET FILS

Rue Hautefeuille, 19, près le boulevard Saint-Germain.

Londres
BAILLIÈRE, TINDALL AND COX.

Madrid
C. BAILLY-BAILLIÈRE.

1879

FIG. 1. Frontispiece of the volume by Bernard, in which the technic of cardiac catheterization is described.

gonflent, et la pression y devient si forte qu'il s'y produit des ruptures et des hémorrhagies.

Mais le point de vue qui nous intéresse le plus est l'étude du cœur par le *cathétérisme*, c'est-à-dire par l'introduction, dans les gros vaisseaux, de sondes que l'on fait pénétrer jusque vers l'organe central de la circulation. Tout le monde connaît les belles expériences par lesquelles Chauveau et Marey ont pu déterminer, en introduisant des sondes dans les oreillettes et les ventricules, les pressions que développent ces cavités lors de leur contraction, et établir avec précision le synchronisme de ces contractions. Ce sont là des types d'opérations de cathétérisme du cœur.

Cathétérisme du cœur. — Pour arriver au cœur nous avons plusieurs routes : d'abord nous pouvons aller dans le *cœur droit* ou dans le *cœur gauche*.

Il est très-facile d'arriver dans le cœur droit (fig. 90, J. K). A cet effet, on fait pénétrer une sonde dans la veine jugulaire, et l'on arrive directement au cœur, puisque la veine cave supérieure n'a pas de valvule. Du reste, la valvule de la cave inférieure n'est pas un obstacle sérieux, et en poussant un peu plus loin la sonde, on peut aller dans la veine cave inférieure.

Il est plus difficile de pénétrer dans le cœur gauche. On s'adresse à cet effet à la carotide, et l'on pénètre par elle jusqu'à l'origine de l'aorte ; mais ici on rencontre les valvules sigmoïdes qui ne sont jamais complétement ouvertes, même au milieu de la systole, ainsi que nous le disions précédemment. Il faut donc quelques tâtonnements et un hasard favorable pour franchir cet obstacle

FIG. 2. Page 277 of the same work, with pertinent paragraphs.

pletely opened, even at mid-systole, as we stated previously. It is necessary, therefore, for some to and fro movements, and a favorable moment to pass the obstacle without rupture. In these cases we must choose preferably the left carotid (Fig. 3) and recline the dog on its right side (we have always performed cardiac catheterization in this animal).

We will specially insist on right heart catheterization, and we will take as the type of operative procedure the performance of this experience in the dog. In this animal the heart is quite mobile. If we recline the dog on his back, the heart displaces posteriorly, or even to a lower position, towards the spine. In this situation it is not easy to get to it. It is necessary to recline the animal on his flank, preferably on his left (Fig. 4) We introduce a lead catheter into the jugular vein, an instrument to which we can give the desired curvature, and which never tears the vessels. We choose a catheter a little thinner than the vein's caliber in order to assure a smooth entrance. To avoid blood losses we pass and adjust a ligature on the vein's wall, over the catheter (Figs. 5 and 6). We smoothly advance this instrument towards the heart, guiding it forward and to the left in order to avoid a wrong passage into the mammaries or azygos veins (Fig. 4). We take care to slightly curve the tip of the catheter, and once we arrive at the level of the heart, we guide it medially, and enter the right atrium.

. . .It is not only important to catheterize the heart, but also to take blood samples at different points of the great arterial and venous trunks: to this effect, it is not practical to open the animal for performing directly a blood-letting on this point of the circulatory system. This procedure causes trouble to the organism, and would have no value for the study of the temperature in the different segments of the circulatory system. It is therefore infinitely better to introduce in this system different catheters of varied nature, according to the investigational purpose (chemical or thermometric research) and get with this instrument to a given and precise point of the preselected vascular cavity. The procedures employed to this pur-

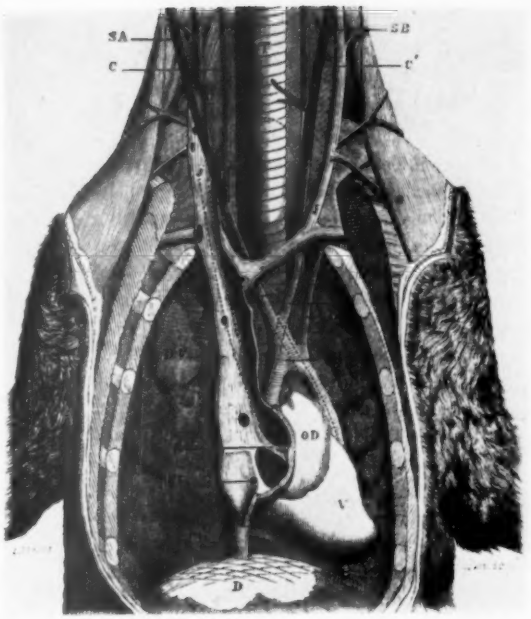

FIG. 3. Figure 90, page 278 of the same work, showing the different routes by which cardiac catheterization can be performed. For right heart catheterization, the catheter, introduced through the jugular vein (J) is represented by the double-dotted line. For left heart catheterization, the catheter (SA) has been introduced through the right carotid (C). OD right atrium; V = right ventricle; DV = superior vena cave; CI = inferior vena cava.

pose derive directly from those which were previously described with cardiac catheterization. In effect, we introduce the catheter through the jugular vein as for right atrial catheterization. In place of turning the catheter's tip medially, we guide it laterally, or downwards, and get to the inferior vena cava. This run is sometimes quite useful, allowing us to descend through this vessel, just to the origin of the renal veins, and also to the level of the iliacs. It is in this way that we can procure venous blood that leaves the corresponding organs, and we already know the value of these types of investigations. We can also use, in place of catheters, thermoelectric needles, obtaining the blood temperature on different points of the venous trunk, at the level of the orifices of the major visceral veins.

In order to perform these different procedures, we can, moreover, choose a directly reversed route, that is to say, ascending from below, through the iliac to the inferior vena cava, and from it to the heart, and also to the superior vena cava and jugular veins. For this purpose, we enter a right or left femoral vein. We usually choose the left, in order to slip into the inferior vena cava, avoiding a pronounced curvature. Once in this vessel, we can push the catheter further, and take blood samples, for instance, above and below the orifice of the renal veins, in order to investigate the differences of the venous blood before and after the outlet of these veins. We can, lastly, arrive at the heart. During vena cava catheterization from below, we are sometimes stopped at the ampulae situated in the inferior vena cava, at the level of the orifices of the hepatic veins. But, as these ampulae are situated on the vein's left wall, we can surely avoid them, entering the venous system through the left femoral vein. . .On the contrary, if we wish to enter the arterial system from below, it is preferable to use the right femoral artery. It is easy to understand, according to vascular topography, that the catheter entering from this side has a less pronounced curvature in its course to arrive to the aorta, and be advanced through it.

We have, therefore, two ways to arrive at the heart, and obtain blood samples from the atria. When the catheter is in the right heart, and its extremity is

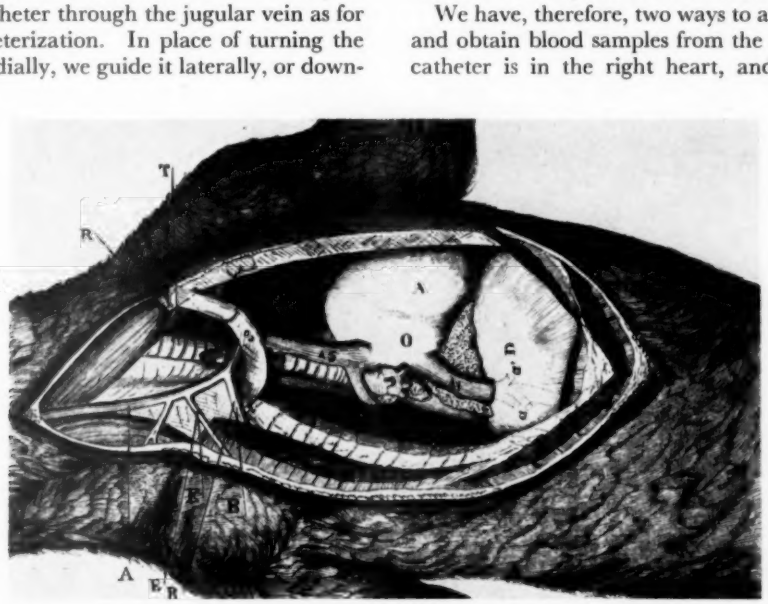

FIG. 4. Figure 92, page 280. Legend as follows: "Heart and caval veins (of the dog); topographic anatomy for catheterization of the heart and great vessels."

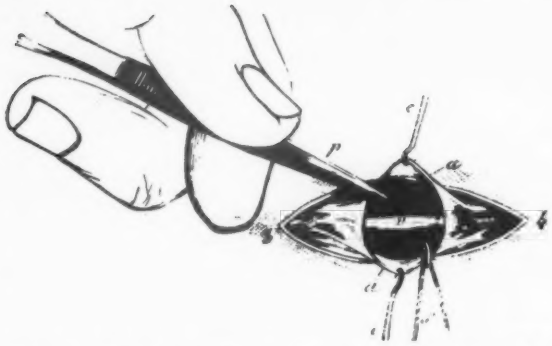

FIG. 5. Fig. 85, same work. Procedure for isolation of a vessel for catheterization purposes.

open, the blood jets with pulsations, under the influence of cardiac contractions. If the catheter was introduced through the jugular vein, it has more freedom of motion, and we see it to beat. . . .

* * *

COMMENTS

Claude Bernard was born on July 12, 1813, the son of Pierre Jean François Bernard, and Jeanne Saulnier.[4] His father was a modest but cultivated man, and to increase his meager income, became a teacher. Bernard began his studies at the age of eight, with a course in Latin, and later geometry, Greek, arithmetic and French. When he was eighteen, his family was unable to support him, and his studies were consequently interrupted. To earn a living, he entered as a pharmacist's assistant from Vaise, Lyons. This early training in chemistry undoubtedly helped him in his later years as an assistant to Magendie at the Collége de France.

If the scientific life of Bernard is to be described as a succession of uninterrupted discoveries, the basis of his drive perhaps can be found, not only in his ambition to excell, but also in the bitterness of his failures, affecting his poetic and literary endeavors, his marital life and his first contact with professorship.[5]

Bernard's experience in theatrical composition began in 1833, when he produced "The Rose of the Rodan." Its success not only brought a hundred francs, but also the confidence in his talent and led to a further production "Arthur of Bretagne." He wanted it presented in Paris, and for that purpose sought a recommendation to a literary critic. In 1834, Mr. Saint-Marc Girardin, professor of literature at La Sorbonne, received the young Bernard, read the manuscript, and advised: "You have worked in a pharmacy; therefore, you can study medicine. You lack the temperament for a dramatic author." Bernard, understanding his failure, felt hurt at the advice, but followed it. Accordingly, he entered the Faculty of Medicine of Paris, and obtained an internship in the Hôtel Dieu in 1839. During 1841, Bernard had the fortune to contact François Magendie, the Professor of Medicine at the Collége de France. Magendie had a strong temper and an eccentric personality, but he was exceedingly objective and a keen observer. The careful and delicate manual procedures of Bernard impressed him, and Bernard was therefore elected his assistant.

It would be of interest to recall the scientific status of medicine and physiology at that time, and the kind of teaching that was undertaken at the Collége de France. When Magendie began his teaching and research career, in 1808–1809, physiology hardly existed as a separate field. The phenomena of life were interpreted according to the ideas of Bichat, who had died pre-

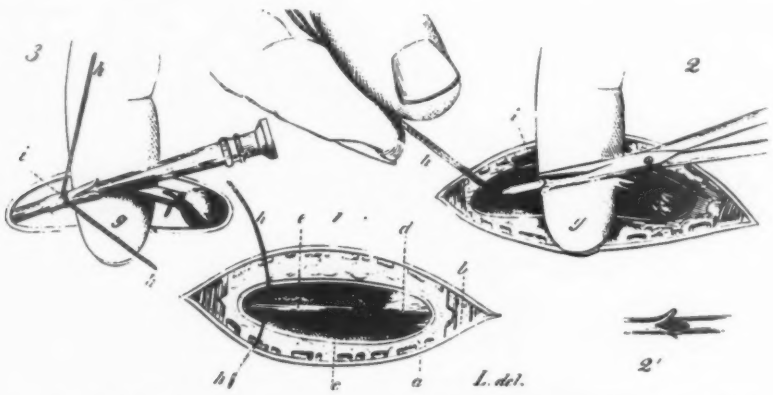

FIG. 6. Fig. 86, same work. Surgical maneuvers for intravenous cannulation. (1) Ligature of the superior part of the vein; (2) incision of the vessel wall, the shape of which is enlarged in 2′; (3) intravenous cannulation and ligature.

maturely in 1802 at the age of thirty-one. An unusually gifted man, he created the fields of general anatomy and histology. He postulated the existence of two qualities: vital and non-vital, belonging to living and non-living things. Determined vital properties corresponded to each system of tissues. The premature passing of Bichat left his work unfinished, and his successors took this simple and schematic biologic system as a guide, leaving aside the experimental method.

When Magendie began his scientific career, the concept of vital properties was growing incessantly, helped by the creative imagination of Bichat's followers. This circumstance explains his peculiar and sometimes excessive repulsion against theories and systematic thinking. Whenever he was questioned on any medical doctrine, he felt a kind of instinctive horror, answering: "Tous cela ne sont que des paroles" (All that is nothing but words). Magendie, however, was an expert investigator, although his avoidance of theoretic disquisitions limited somewhat the planning of his experiments and the magnitude of his contributions.

The young Bernard was not a brilliant student at the Faculty of Medicine, but working with Magendie he made quick progress, and in 1843 he decided to conduct independent research. In 1844 he applied for an assistant professorship at the Faculty of Medicine, presenting as a thesis "Des Matières Colorantes chez l'Homme." He was surpassed by A. Béclard, a less gifted investigator but a more brilliant orator.

Bernard felt for the second time the bitterness of failure. In a fit of depression he nearly abandoned Paris to become a general practitioner in his native town. His friend, Mr. Pelouze, knowing the quality of his intellect and his dexterity as an investigator, tried to retain him in Paris, resorting to the enchantments of marriage. In effect, a few months later Bernard was married to Miss Martin, a physician's daughter, and remained in Paris. It soon became apparent that this woman was not able to share his sacrifices nor to bring him the encouragement necessary in a physiologist's life. Bernard did not find in his home, therefore, the tenderness and rest such an active man needed. All his life he was affected by his marital failure, but he kept going along. In 1847 he was appointed Assistant Professor at the Collége de France and eight years later, following the death of his teacher, he became Professor of Medicine at the same institution. It is pertinent to name some of his predecessors: Vidus Vidius (1542), Sylvius (1550), Riolan (1604), Guy Patin (1654), Tournefort (1703), Astruc (1732), Fenein (1742), Corvisart (1794), Laennec (1822) and Magendie (1831).

The work of Bernard is to be found in his *Leçons* comprising eleven volumes written between 1854 and 1879, and his scientific philosophy in the "Introduction à l'Étude de la Médicine Expérimentale." The reading of his volume on "Physiologie Opératoire" is quite instructive, even today. It is appropriate to remember that Bernard employed, with the help of D'Arsonval, thermoelectric needles for the measurement of temperature differences of venous and arterial blood. Curarization and tracheal intubation were also employed in his laboratory.

It was said of him: "The distinction of his person and the noble beauty of his physiognomy seduce immediately. No pedantry, no eccentricity, and the most simple and natural conversation, beyond all affectation, but full of right and deep judgment, these are some of the external traits of Claude Bernard." These are the words of Louis Pasteur.[6]

References

1. Crowe, S. J. Halsted of Johns Hopkins. The Man and his Men, p. 88. Springfield, Ill., 1957. Charles C Thomas.
2. Lain Entralgo, P. Dos Biológos: Claudio Bernard y Santiago Ramón y Cajal, pp. 97–98. Buenos Aires, 1949. Espasa-Calpe.
3. Bernard, C. Leçons de Physiologie Operatoire, pp. 277–286. Paris, 1879. Ballière.
4. Olmsted, J. M. D. Claudio Bernard, Fisiólogo (Spanish translation), pp. 17–18. Buenos Aires, 1951. Peuser.
5. Lain Entralgo, P. Colección Clásicos de la Medicina: Claudio Bernard, pp. 7–12. Madrid, 1947. El Centauro.
6. Pasteur, L. Claude Bernard. Idea de la importancia de sus trabajos, de su enseñanza, y de su método. Reproduced in: Claude Bernard: El Método Experimental y Otras Páginas Filosóficas, pp. 187–192. Buenos Aires, 1947. Espasa-Calpe.

Diagnostic Shelf

Mitral Stenosis or Rheumatic Carditis?

A. A. Luisada, M.D., F.A.C.C. *and* J. Szatkowski, M.D.

Chicago, Illinois

An eighteen year old white girl, a student nurse, was first seen in the Emergency Room of the Hospital in September 1957 because of paroxysmal shortness of breath, chest pain and non-productive cough, which developed after playing tennis.

Her past history was non-contributory with the exception of frequent sore throats; there was no history of rheumatic fever. On routine examination, mitral stenosis had been diagnosed in May 1957.

In November 1957, after playing baseball, severe dyspnea, orthopnea and chest pain developed again. The patient was then hospitalized and treated with bedrest and the administration of oxygen.

PHYSICAL EXAMINATION

Examination revealed a normally developed girl. Blood pressure was 120/70 mm. Hg.; pulse rate, 80/minute and regular. An apical impulse was noted in the fifth intercostal space in the midclavicular line. There was a loud and snapping first apical sound. A presystolic crescendo murmur, louder in the left lateral decubitus, and a grade 3 blowing systolic murmur radiating to the axilla, were heard at the apex.

The laboratory findings were non-contributory (including ASO titer, C-reactive protein and sedimentation rate).

Electrocardiogram showed left axis deviation. Otherwise, the tracing was normal.

Roentgenogram of the chest revealed a prominent pulmonary artery and a normal left atrium.

The patient was discharged on the third hospital day. Because of frequent sore throats, she underwent tonsillectomy and later on, in March 1958, the patient was submitted to both right and left heart catheterization.

PHONOCARDIOGRAMS

The *phonocardiogram* on the first admission (Fig. 1) revealed a presystolic murmur in crescendo and a high-pitched systolic murmur in decrescendo at the apex; possible opening snap followed by a third sound was also recorded at the apex, and a split second sound was recorded at the base.

While the systolic murmur, the third sound,

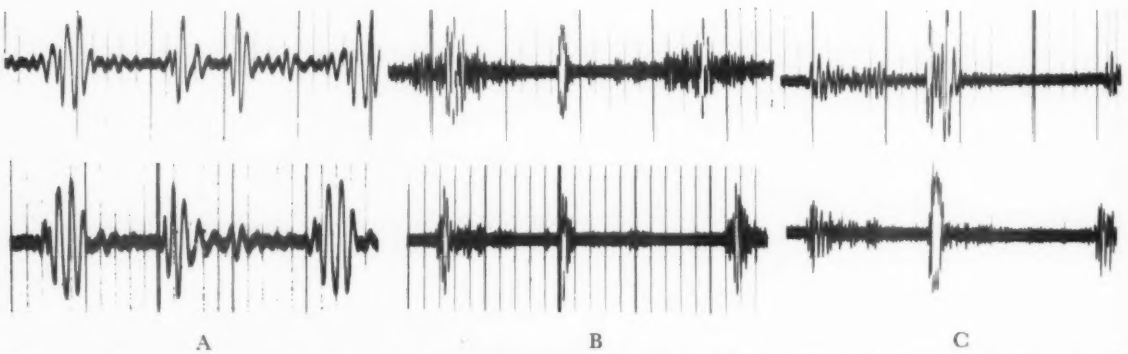

Fig. 1. Phonocardiograms of patient *Top*, November 1957. *Bottom*, March 1958. A, apex, band 30–60. B, midprecordium, band 120–240. C, pulmonic area, band 120–240.

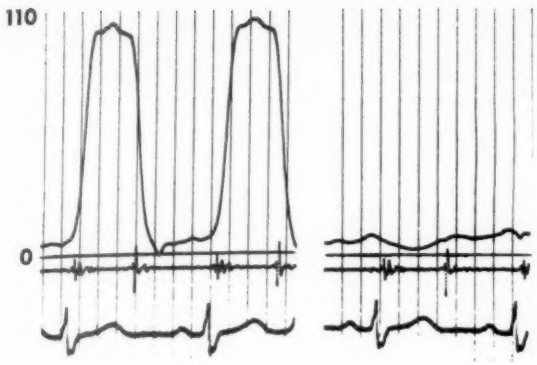

FIG. 2. Left heart pressures. A, left ventricle. B, left atrium, in a pullback (for clarity, a section containing three premature beats has been cut out).

and the left axis deviation could be interpreted as evidence of mitral insufficiency, the presystolic murmur and the opening snap, if this small vibration was correctly interpreted, would indicate mitral stenosis. On the other hand, all these data were too sharply evident to be considered the result of a combined stenosis and insufficiency. Therefore, both for diagnosis and for possible surgical implication, cardiac catheterization was suggested.

The patient returned for catheterization five months later. At that time, a new *phonocardiogram* (Fig. 1) revealed only a minimal systolic murmur; no presystolic murmur, no opening snap and a smaller third sound.

CARDIAC CATHETERIZATION

Right heart catheterization revealed a right ventricular pressure of 30/2.5-6.8 mm. and a pulmonary arterial pressure of 27/10.7 mm. These were considered borderline figures and were not consistent with a significant mitral lesion.

Left heart catheterization revealed a mean left atrial pressure of 8.1 mm., a left ventricular pressure of 110/1.35, and an aortic pressure of 110/66 mm. A minimal gradient of 3 mm. was present between the left atrium and left ventricle. This was considered as the result of minimal mitral stenosis. The left atrial pattern was perfectly normal (Fig. 2) and there was no regurgitant wave. *Intracardiac phonocardiography* of the left chambers revealed no murmurs.

The final conclusion was that the patient had a minimal mitral valvular narrowing due to rheumatic fever and that an *acute carditis*, caused by unrecognized recurrence of rheumatic fever, had been responsible for the loud presystolic and systolic murmurs. Obviously, no surgery was recommended.

Acute carditis is sometimes present even when all laboratory data are non-contributory.

Readers are invited to submit reports of interesting cases and illustrative tracings for this department. These should not exceed 1,000 words in length. Although not necessarily original, all material submitted should have teaching value.

Progress Notes in Cardiology

Edited by EMANUEL GOLDBERGER, M.D., F.A.C.C.
New York, New York

Adrenal-Regeneration Hypertension

A SYNDROME of hypertensive vascular disease occurs in the young female rat during regeneration of the adrenal cortex when the mass of renal tissue has been reduced by unilateral nephrectomy and the intake of sodium chloride has been increased by placing the animal on 1 per cent saline drinking solution. If any one of these conditions is omitted the syndrome fails to develop. This emphasizes their fundamental pathogenetic importance, but does not indicate their mechanism of action. It is this latter problem which requires solution in the case of each condition. An interesting review of this entire problem has recently been presented by Floyd R. Skelton (*Physiol. Rev.*, 39: 162, 1959).

The similarity between the hypertensive disease induced by adrenal regeneration and by exogenous steroid administration under similar experimental conditions has led to the following suggestions as to the way in which the regenerating cortex might produce the hypertensive state: (1) increased secretion of glucocorticoids (presumably corticosterone) at some stage of regeneration; (2) imbalance (only temporary, perhaps) between secretion of corticosterone and aldosterone; (3) secretion of some abnormal and presently unknown steroid; and (4) sensitization to subsequently secreted adrenal corticoids by the period of adrenal insufficiency which follows the enucleation procedure. None of these mechanisms has been established or ruled out by presently available evidence. However, the onset of hypertension between the second and third week after enucleation, and the observation that plasma-free corticosteroids may reach super-normal levels during the same period, may be more than coincidental.

The association of sodium chloride intake and the development of hypertension during adrenal regeneration is similar to that observed in hypertension induced by various steroid hormones. In this regard the most important questions have to do with the retention and distribution of sodium within the body rather than with simply how much sodium is consumed. Studies to answer these questions remain to be made. Perhaps the reduction of the renal mass, which is necessary for adrenal-regeneration hypertension to occur, acts by reducing the capacity for sodium excretion.

Once hypertension has been established, neither removal of the regenerated adrenal nor substitution of water for saline drinking fluid regularly brings about a decline in blood pressure. Similar observations have been noted in severe human systemic hypertension (Goldberger, E.: *Am. J. Cardiol.*, 1: 154, 1958).

Thromboembolism of the Lungs

THE INCIDENCE of thromboembolism of the lung of either surgical or medical origin has remained high in spite of greater clinical awareness and better methods of prevention, vein ligation and anticoagulant treatment. The clinical signs and symptoms are frequently suggestive. However, roentgenography or angiocardiography is decisive in a high percentage of cases. This has been shown in a recent paper by Drs. Julian Arendt and Max Rosenberg (*Am. J. Roentgenol.*, 81: 245, 1959).

Thromboembolism without infarction is seen as an abnormal transparency of the involved segment of the lung (Westermark sign) with absence of one or both of the large hilar vessels. The heart shadow assumes a peculiar shape, best described as the "amphoric" type. In the absence of both hilar vessels (pulmonary arteries), a large saddle embolus must be considered.

A thrombus or embolus, which is located slightly more peripherally within the main

branches of the pulmonary arteries, causes a buckling and aneurysmal widening of the vessel, with either a sharp cut-off or tapering at the peripheral end of the embolus. Such thrombus or embolus is compatible with life, and leads to the development of either acute or chronic cor pulmonale. In contrast to the cor pulmonale of obstructive emphysema, the position of the diaphragm is elevated and the heart does not assume the vertical position. In addition enlargement of inflow and outflow tracts of the right ventricle develops within a short time.

Thromboembolism with infarction does not, as a rule, show Westermark's sign of increased translucency of a lung segment, since it occurs mostly in a congested lung with dilated bronchial arteries and numerous collaterals. Infarction is common in mitral stenosis, hypertensive heart failure and coronary insufficiency. Infarcts represent areas of ischemic necrosis usually located at the periphery of the lung. They are rarely "wedge-shaped," as the apex of the wedge is cut off. A "truncated cone" or an "umbrella" shape results which is quite characteristic. Smaller infarcts frequently have a cuboid or meniscus-like appearance. In the costophrenic angle the "hump-shaped" elevation on the medial side of a small pleurisy has frequently been observed and appears diagnostic. The base of an embolic infarct is sometimes the interlobar fissure line, along which it forms a parabolic shadow, which is best seen on a lateral roentgenogram.

Cardiac Resuscitation

Edited by PALUEL J. FLAGG, M.D., F.A.C.C.*

New York, New York

Drugs in Cardiac Resuscitation

IN A PREVIOUS chapter the physiology of the heart beat was briefly reviewed. Now let us consider, with equal brevity, the effect of acetylcholine, epinephrine and procaine (with its amide, Pronestyl) upon the normal physiology of the cardiovascular system. The use and effect of drugs in cardiac resuscitation are familiar to the internist. His diagnostic skill allows him to pinpoint the target and to enlist the resources of pharmacology.

Acetylcholine and epinephrine clearly imitate the action of the vagus and sympathetic nerves. They are actually produced by stimulation of these nerves, vagus stimulation yielding acetylcholine, and sympathetic stimulation, epinephrine.

Acetylcholine: The typical cardiovascular responses to acetylcholine are: (1) vasodilation; (2) fall in blood pressure; and (3) bradycardia, partial or complete heart block and ventricular standstill of varying duration. Since acetylcholine is rapidly destroyed in the body, these effects depend on the dose and site of application.

Epinephrine: The effects of epinephrine are directly opposite to those of acetylcholine: (1) the heart rate is accelerated; (2) the cardiac output is enhanced; (3) the tone of the heart and force of contraction are increased; (4) cardiac systole is shortened; (5) the work of the heart is increased; and (6) oxygen consumption is increased.

Epinephrine acts directly on the myocardium, independently of alteration in cardiac function, which is secondary to the effect of epinephrine on the peripheral circulation. In addition to the tachycardia, epinephrine may cause increased myocardial irritability.

Premature ventricular systoles may occur and may be the precursors of more serious ventricular arrhythmias, or fibrillation. If present, other factors such as anesthesia (chloroform, cyclopropane) may increase cardiac irritability. Epinephrine is too often looked upon as an effective agent in reviving patients apparently dead from drowning, electrocution, anesthetic agents, etc. Although the drug occasionally produces dramatic results, more often it fails entirely. Frequently the heart is already either beyond resuscitation or in ventricular fibrillation from the injected epinephrine.

If heart sounds are unobtainable, 0.2 to 0.3 cc. of a 1:1,000 solution (diluted tenfold) may be injected, preferably into the right atrium or right jugular vein. If the heart is exposed and found flabby, unresponsive to massage and not in ventricular fibrillation, the epinephrine should be infiltrated directly into the myocardium.

If asystole occurs during inhalation anesthesia, as with chloroform, cyclopropane or trichlorethylene, quite possibly ventricular fibrillation already exists, and little benefit can be expected from epinephrine, which does not stop fibrillation. For this situation direct massage of the exposed heart and artificial respiration with 100 per cent oxygen should be employed first. If the heart is in ventricular fibrillation, electrical defibrillation must be attempted, but if cardiac arrest occurs without ventricular fibrillation, electrical countershock is contraindicated.

Procaine: Procaine elevates the threshold of the ventricular muscle to electrical stimulation. The short duration of action resulting from its

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rapid enzymatic hydrolysis and its prominent central nervous system effects limit the therapeutic value of procaine as an antifibrillatory and antiarrhythmiac agent. Procaine amide (Pronestyl) is a more effective agent to prevent or control tachycardia. Procaine amide hydrochloride U.S.P. is supplied in 10 ml. vials containing 100 mg. per ml., for intramuscular and intravenous injection. Its duration of action is more satisfactory and the relationships between cardiac and central nervous system effects are more favorable than procaine.

Procaine amide (Pronestyl) depresses the excitability of both atrium and ventricle to electrical stimulation and slows conduction in the atria, the bundle of His and ventricles.

Ventricular extrasystoles, caused by blockage of the coronary arteries, are suppressed.

The prophylactic and therapeutic value of procaine amide for reducing the incidence and severity of arrhythmias encountered during cardiac surgery is well proved. The intravenous dose of Pronestyl is 200 to 500 mg. (occasionally as high as 1.0 Gm.) administered at a rate not exceeding 25 to 50 mg. per minute. Severe hypotension is a drawback and should be watched for carefully.

For fibrillation the drug may be given intracardially; massage should be continued and 100 per cent oxygen administered. Epinephrine under these conditions has a place in rendering a flabby ventricle more firm and improving the arterial pressure evoked by cardiac compression. But epinephrine itself does not defibrillate the dog's heart, even with massage, and time should not be wasted in trying to stop fibrillating human hearts with epinephrine.

Procaine or Pronestyl may be given, but the only really effective way to defibrillate the heart is by electrical countershock. The importance of creating a uniform state of depolarization in all muscle fibers by this procedure is to be emphasized.

Oxygen: Effective cardiac massage, as judged by maintaining the mean arterial pressure, must be supported by 100 per cent oxygen to insure a supply of oxygenated blood to the myocardium. Electrical stimulation is useless unless it is done before the heart is blue. Epinephrine and Pronestyl are much more likely to be effective if oxygen is distributed equally throughout the heart muscle. Areas of anoxia in the myocardium apparently set up electrical potentials which continue the discharge of stimuli from ectopic foci.

Summary

In cardiac resuscitation we are concerned with the effects of three drugs: acetylcholine, epinephrine and procaine. Acetylcholine is formed by vagal stimulation. Its effects in the experimental animal are dramatic: a few drops on the surface of the heart and the heart stops beating. Atropine is a direct antagonist: a few drops on the arrested heart and it resumes beating.

The success or failure of resuscitation of the heart depends upon oxygen. Attempts to defibrillate the heart, by external means, after a period of sixty seconds will be unsuccessful because of the accumulated hypoxia unless oxygen is used also.

In cardiac resuscitation the physician must respond reflexly. There is no time for a choice from a number of drugs. Consider and act on only two—epinephrine and procaine. Epinephrine—dilute the stock solution, 1 cc. of 1:1,000, with 10 cc. saline. Administer small repeated doses. The drug acts like a whip to increase the tone, vigor and rate of contractions of a flabby myocardium. Oxygen must be present for effective results. The temporary metabolic deficit caused by rapid use of oxygen must be faced in this temporary emergency by using endotracheal oxygen under pressure.

Procaine depresses the myocardium and helps to defibrillate a highly irritable heart. The use of a 0.25 to 0.5 per cent solution must be accompanied by electrical defibrillation.

Workmen's Compensation for the Cardiac

Coronary Arteriosclerosis as an Underlying Cause of an Acute Cardiac Insult

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IN this paper we will discuss the third question which the Morland Commission submitted to a number of doctors for the study of compensation in cardiac disability due to strain.[1] The question reads as follows:

"*Is it your opinion that a workman who suffered a coronary closure and infarction of the heart must have had a pre-existing coronary arteriosclerosis?*"

Of 397 internists and cardiologists who answered the question, 361 or 90.9 per cent said yes or yes with rare exceptions and 36 or 9.1 per cent said no or no with some exceptions. Some of those who answered yes with exceptions believed that occasionally other diseases of the coronary arteries may produce myocardial infarction, such as coronary embolization, coronary arteritis, thromboangiitis obliterans, periarteritis nodosa and syphilitic coronary ostial stenosis. Also, conditions other than coronary disease, such as anemia, hemorrhage and shock due to any cause, may at times precipitate myocardial infarction.

My personal opinion is that coronary atherosclerosis is a necessary background for the development of an acute coronary episode. Exceptions are those mentioned to which may be added cardiac hypertrophy and prolonged cardiac arrhythmia with rapid ventricular rate. With these exceptions, and in many instances in the presence of these conditions, all cases of an acute cardiac insult reveal evidence of a greater or lesser degree of coronary atherosclerosis at autopsy. It is interesting to find, however, that in a good many such cases no complete occlusion of a coronary artery will be found in the presence of infarction, and in others no infarction will be found in the presence of occlusion. It is also important to observe that many cases of sudden death from an acute cardiac insult will reveal neither complete occlusion nor infarction, death being due apparently to either cardiac arrest, ventricular fibrillation or heart failure. The question as submitted by the Morland Commission may therefore be considered rather narrow, and certainly does not apply to all individuals who suffer an acute cardiac insult.

Relation Between Coronary Atherosclerosis and Myocardial Infarction

It must be understood that the mere presence of pre-existing coronary atherosclerosis is not the sole cause of either a myocardial infarction or any other acute cardiac insult. This is evidenced by the fact that in some cases of infarction, focal necrosis or sudden cardiac death, the coronary arteries may show relatively little atherosclerosis. Gross and Sternberg[2] have reported fifteen autopsy cases of myocardial infarction without significant coronary atherosclerosis. They attributed the condition to prolonged coronary vasospasm, tachycardia, shock, severe anemia, polycythemia and possible humoral elements, such as excessive secretion of epinephrine or other vasopressor substances. Most of their patients had hypertension and cardiac hypertrophy. Valvular disease with associated cardiac hypertrophy may also predispose

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to infarction under such circumstances even in the absence of gross coronary atherosclerosis.

Relation Between Work and Coronary Atherosclerosis

The question "Will coronary arteriosclerosis develop during certain types of work over a short period of time?" may be answered in the negative. In a previous report[3] on cardiac disability caused by strain, I included among several cases the instance of a 31 year old seaman who was working on board a gasoline transport freighter at sea. During a long trip of about three weeks, he had worked arduously cleaning large empty gasoline tanks and chipping off old paint with a heavy hammer. The air in the tanks had a heavy gasoline odor and his sleeping quarters had poor ventilation. While doing his work he experienced intermittent oppression of the anterior part of his chest, and at night he was awakened from his sleep by severe chest pain lasting one hour, which recurred periodically during the rest of the trip to and from New York. When he finally reached shore, a doctor who examined him advised hospitalization. He remained in the hospital several weeks where repeated electrocardiograms revealed evidence of myocardial ischemia shifting in various areas and a small area of posterior left ventricular infarction. He was finally discharged from the hospital in relatively good condition, the electrocardiogram showing only residual myocardial damage. He was asymptomatic and was able to return to lighter work. My impression was that the strenuous activities together with improper hygienic conditions produced acute coronary changes with myocardial ischemia and infarction in the presence of latent asymptomatic, pre-existing coronary arteriosclerosis.

An editorial comment by the editors of the textbook "Trauma and Disease,"[4] in referring to this case expressed the belief that it is possible that the daytime work in which the seaman was engaged prior to his anginal attack had something to do with the progress of the disease but it is a "gross overstatement" of the situation to draw my conclusions. Evidently the editors believed that there was pre-existing coronary disease in this case and the recurring attacks of pain and the myocardial changes might have been spontaneous and not related to the work.

On the other hand, I received many comments from other men in different parts of the country, who believed that the onset of the acute anatomic coronary changes and insufficiency in that case could have been directly the result of the work and environment without any pre-existing coronary disease. For example, one of the letters received from a prominent clinician in a mid-western state said, in part, the following:

> "It seems to me one of the central issues in this problem is the question of whether or not physical and/or emotional effort, especially of a continuing type, may be the initiating or even etiologic factor in the production of some cases of coronary disease. . . . You apparently assume that work effort can precipitate coronary episodes only in the presence of pre-existing disease. An example is the case of the seaman who had symptoms apparently resulting from strenuous work under poor hygienic conditions. You state here that his condition occurred 'in the presence of latent asymptomatic pre-existing coronary disease.' How can you justify such a broad assumption and could not such working conditions cause the symptoms described, by precipitating an acute coronary insufficiency with vasospasm, etc., in a person whose coronary arteries are perfectly normal?. . . And should a worker be faced with this kind of environmental exposure day after day over a long period of time, could not this in itself be the precipitating factor of intimal hemorrhage and the other ingredients which would eventually add up to coronary artery disease? It seems to me that we will make further progress in elucidating the problems of coronary heart disease, if we recognize that the heart, like any other part of the body, is not immune to environmental influences and that some of our answers may lie in this direction. The question of workmen's compensation is an economic one and irrelevant in any scientific discussion of the problem. Unfortunately, too often this aspect colors the attitudes of physicians and others who may be quite scientific in their approach to other medical problems."

Evidence for Pre-existing Coronary Atherosclerosis

My opinion that some pre-existing coronary atherosclerosis in this seaman was a necessary prerequisite for the development of the acute coronary and myocardial manifestations was based on the following reasons: (1) For angiospasm of coronary arteries to occur, as for other arteries of the body, some atherosclerosis or other diseased process in the vessel must be present. No prolonged angiospasm has been demonstrated to take place in a perfectly normal blood vessel. (2) As discussed previously,[5] the development of atherosclerosis is slow, perhaps over a period of years, and appears to be initiated by recurring hemodynamic changes

of the coronary circulation. (3) Acute pathologic changes of the coronary arteries are always found to be superimposed on old atherosclerotic areas which pre-existed. (4) The clinical manifestations of coronary disease begin to exhibit themselves in most cases only when the atherosclerotic process has reached an advanced stage, when the blood supply to the myocardium is interfered with, or when sudden acute anatomic changes develop suddenly in a coronary atheromatous plaque. Enos and co-workers[6] found that more than 77 per cent of the people who died accidentally in the 18- to 48-year age group showed evidence of a greater or lesser degree of coronary atherosclerosis at autopsy. This would further substantiate the impression that atherosclerosis of the coronary arteries precedes acute coronary attacks.

The theory that clinical manifestations of coronary insufficiency or of an acute cardiac insult occurring during prolonged work such as was exemplified by the seaman mentioned is a "gross overstatement" can, I believe, be entirely refuted. Here was an individual who experienced recurring chest pain while working arduously over a period of three weeks under unhealthy conditions, which was finally diagnosed electrocardiographically as diffuse coronary insufficiency and focal necrosis of the posterior wall of the left ventricle. It does not require any unusual imagination to assume that progressive acute anatomic coronary changes had taken place during this period which resulted in the myocardial involvement. To argue that coronary insufficiency occurred here spontaneously is to deny that for insufficiency to occur there must be some known cause, besides the presence of pre-existing coronary atherosclerosis. That we do not always discover the cause does not speak for spontaneity of an attack but for our inefficient diagnostic acumen or the lack of known established causes, as discussed in a previous report.[7] When causes are clearly discernible such as in this case, we certainly have no right to deny them.

Summary

Pre-existing coronary atherosclerosis is a necessary requisite for the development of acute coronary and myocardial changes under certain conditions. There are, however, various relatively rare diseases of the coronary arteries that may also precipitate acute cardiac changes. Extracoronary factors, such as anemia, polycythemia, hemorrhage, shock, extreme tachycardia and arrhythmia and cardiac hypertrophy, may at times produce acute myocardial changes in the absence of gross coronary disease. An acute cardiac insult developing in the absence of these extracoronary factors and, in many cases in their presence, is to be attributable to a sudden acceleration of a chronic atherosclerotic process in the coronary arteries.

References

1. Sigler, L. H. Results of a questionnaire on relation of exertion to myocardial infarction. *Am. J. Cardiol.*, 2: 781, 1958.
2. Gross, H. and Sternberg, W. H. Myocardial infarction without significant lesions of coronary arteries. *Arch. Int. Med.*, 64: 249, 1939.
3. Sigler, L. H. Cardiac disability and death caused by strain: problem in workmen's compensation. *J. A. M. A.*, 154: 294, 1954.
4. Moritz, A. R. and Helberg, D. S. Trauma and Disease, Selections from the Recent Literature. Central Book Co., Inc. 1959.
5. Sigler, L. H. Relationship of work to heart disease. *Am. J. Cardiol.*, 3: 261, 1959.
6. Enos, W. F., Holmes, R. H. and Beyer, J. Coronary disease among United States soldiers killed in action in Korea. *J. A. M. A.*, 152: 1090, 1953.
7. Sigler, L. H.: Relationship of strain to an acute cardiac insult. *Am. J. Cardiol.*, 4:261, 1959.

The Query Corner

READERS are invited to submit queries on all aspects of cardiovascular diseases. Insofar as possible these will be answered in this column by competent authorities. The replies will not necessarily represent the opinions of the American College of Cardiology, the JOURNAL or any medical organization or group, unless stated. Anonymous communications and queries on postcards will not be answered. Every letter must contain the writer's name and address, but these will not be published.

Death of Monkey, Able

Query: The monkey, Able, when prepared for flight was expendable and replaceable. The vastly complicated and costly program involved transformed her into an international figure of supreme scientific importance, unique and irreplaceable. We would appreciate a comment on the reported sudden circulatory collapse under anesthesia and the unsuccessful attempts at resuscitation.

Answer: Pending an official medical review of this anesthetic accident, the following facts invite consideration. The surgical procedure, although slight, called for general anesthesia—pain control *with* unconsciousness. Analgesia—pain control *without* loss of consciousness, is impractical in animal surgery.

While trichlorethylene (the reported anesthetic) is frequently used as an *analgesic*, it is *not* recommended as a *general anesthetic*, even in therapeutic doses. "Cardiac arrhythmias of a serious nature and multifocal ventricular tachycardia [occur]—[there is a] high incidence of serious cardiac irregularities; [it] sensitizes the myocardium to sympathoadrenal discharge." (GOODMAN and GILMAN: The Pharmacological Basis of Therapeutics, 2nd ed., p. 71. New York, 1955. Macmillan.) The action of trichlorethylene parallels that of chloroform and cyclopropane.

If these intrinsic hazards were justified and accepted, their occurrence and development were to be anticipated. They should have occasioned no surprise. Such anticipation called for the *immediate* recognition of cardiac failure and the availability of the most efficient method of respiratory and cardiac resuscitation.

Mouth-to-mouth artificial respiration is presently recognized as the first aid method of choice. It is out of place in the operating room. Such practice suggests that the operator is unfamiliar with resuscitation at the professional level, i.e., laryngoscopy, intubation and insufflation of oxygen under measured pressure. (See *Am. J. Cardiol.*, 2: 513, 1958.) Since cardiac arrest or fibrillation is immediately followed by complete flaccidity, intubation is easily accomplished and provides prompt oxygenation of the circulation. Oxygenation under pressure is necessary in cardiac massage and mandatory for recovery in fibrillation. The press reports suggest ventricular fibrillation. Respirocardiac failure from this cause demands immediate laryngoscopy and intubation following collapse of the blood pressure. No time is to be lost in seeking corroborative signs of cardiac standstill. The heart is to be exposed at once and massaged. When blood pressure recovers, the heart is to be examined closely for fibrillation or the return of a normal beat. The brain having been protected from hypoxia, and the circulation reestablished, the emergency is over. The problem is then one of postoperative care.

It may be presumed that in the case of Able, ether, which presents no cardiac hazards, a laryngoscope, endotracheal tubes and a defibrillator were present. When the medical report is released, an explanation covering the choice of the anesthetic and the resuscitation technic employed will doubtless become available.

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Book Reviews

Atrial Arrhythmias, Digitalis and Potassium, by Bernard Lown and Harold D. Levine. Landsberger Medical Books, Inc., New York, 1958, pp. 222, illus. 53, $6.90.

In this short monograph the authors have brought together data collected from the literature, as well as their own clinical and electrocardiographic observations, concerning the etiology and treatment of a type of auricular arrhythmia which is considered a distinct electrocardiographic entity, and designated as "paroxysmal atrial tachycardia (P.A.T.) with block." Extensive clinical and some experimental data are presented to support the concept that "digitalis may be an important factor in the genesis of P.A.T. with block." Some of the problems concerned with the differential diagnosis of P.A.T. with block are discussed, and the authors conclude that the condition can be characterized by an ectopic atrial arrhythmia ranging from 150 to 200, with small upright P waves in the extremity leads; frequently inconstant P-P interval; and various types of atrioventricular block. In addition, carotid sinus stimulation results in increased A-V block without much change in auricular rate.

The authors emphasize again the fundamental importance of potassium equilibrium in the body in regard to digitalis action, and it is concluded that this condition is fundamentally the result of potassium depletion of the heart. Moreover, this condition is associated with a high mortality and requires prompt treatment. From the point of view of treatment, it is recommended that digitalis should be withheld, and all medication which can lead to potassium loss similarly restricted. Administrations of potassium salts combined with procaine amide are considered effective in controlling P.A.T. with block. Finally, some preliminary observations regarding the value of induced hypocalcemia by intravenous injection of the chelating agent, sodium ethylene diamine tetra-acetic acid (Na-EDTA), are also presented.

Although the possible role of potassium loss in digitalis action is not new, the book is a clearly written presentation of the authors' concepts and should be useful to all cardiologists.

K. I. Melville, M.D.

Vascular Surgery, by Geza de Takats. W. B. Saunders Co., Philadelphia, 1959, pp. 726, $17.50.

This is a well organized and necessary book. It is clear, cogent and comprehensive.

The rich experience of the author is evident throughout most of the text. The reader rarely feels that he is being given simply a survey of the literature despite the pertinent and full bibliography at the end of each section.

It is unfortunate that the traditional word "thromboembolism" appears as the heading of an important chapter. This results in a lack of clarity in the presentation of embolic and thrombotic occlusions of the peripheral arterial tree.

This volume must find its way to the book shelf not only of the surgeon but also of the internist deeply interested in vascular disease.

Lester Blum, M.D.

Nutrition and Atherosclerosis, by Louis N. Katz, Jeremiah Stamler and Ruth Pick. Lea & Febiger, Philadelphia, 1958, pp. 146, $5.00.

The relationship between diet and the development of atherosclerosis is the subject of a provocative book by Drs. Katz, Stamler and Pick. These investigators are among the more articulate proponents of the theory that a high fat-high cholesterol diet is the decisive factor in the causation of hypercholesteremia and atherogenesis.

In presenting their thesis the authors draw upon findings from the pathologic and clinical laboratories, from the experimental animal, from limited controlled experiments in man, and from epidemiologic studies of populations in various parts of the world. They have assembled an excellent bibliography, included in which are their own extensive and original investigations.

Proof of the interrelationship of diet, serum cholesterol level and deposition of lipid in atheromatous plaques in man is dependent upon a number of pieces of indirect evidence. The important points are as follows: (1) the atheromatous plaque in the arterial intima consists primarily of cholesterol; (2) athero-

matosis is more extensive in clinical conditions in which there is hypercholesteremia; (3) hypercholesteremia and the deposition of lipid in the arterial intima can be induced in certain laboratory animals by feeding cholesterol; (4) population studies indicate that where the average serum cholesterol level is low (the Bantus or Japanese) the incidence of coronary atherosclerosis is low, and where the average level is high (the Americans or British) the incidence of coronary disease is also high; (5) sharp restriction of fat in the human diet lowers the average serum cholesterol level; and (6) the fat-restricted diet in occupied European countries in wartime was accompanied by a drop in the incidence of coronary atherosclerosis.

These points are documented clearly and completely with frequent references to charts, graphs and diagrams reproduced from the original publications, and their elucidation occupies the main portion of the work. The authors then point out that other factors (genetic, endocrine, emotional, physical, etc.) are also involved in the metabolic derangement by which atherosclerosis is produced, but that these factors are secondary in importance to the nutritional problem. They conclude that if a high fat diet were not ingested habitually, no other factor or combination of factors could produce a significant degree of atherosclerosis.

The style of writing is pleasing and the material reads easily. The illustrative graphs and diagrams are well chosen. The recent literature has been admirably compiled. This book will be of value to most internists and cardiologists, especially to those interested in this particular subject. It can be recommended to anyone who wishes to embrace the "fatty diet produces hypercholesteremia produces atherosclerosis" theory; and to those who desire a guide to the literature of the entire field of atherosclerosis and lipid metabolism.

However, many authorities do not subscribe as heartily to the nutritional theory as do Katz and his co-authors. Since the text primarily discusses only one side of the question, students or practitioners not familiar with the large body of evidence which indicates that diet is perhaps not the decisive factor in atherogenesis may be misled.

In fairness to the total problem, the authors do not emphasize strongly enough the cardinal principle involved—namely that there is not a single adequately-controlled study in man which indicates that the specific lowering of serum cholesterol, by dieting or any other means, affects the subsequent development of atherosclerosis. After carefully building their case for the prime role played by diet in atherogenesis, they indicate that dietary restrictions directed at reducing serum cholesterol levels need not be difficult to accomplish or unpleasing to the taste.

Unfortunately, moderate dietary manipulation will not affect the serum cholesterol level to any marked degree in most instances. In order to accomplish a significant lowering of serum cholesterol, either a rigid fat-free diet must be followed or a diet must be employed in which the ratio of unsaturated to saturated fat is at least 3 to 1. Diets of this type are not easily planned nor are they particularly pleasing to the taste.

Despite its deficiencies, however, this book should be read by everyone interested in the general problem. LOUIS E. SCHAEFER M.D.

Cholesterol, by David Kritchevsky. John Wiley & Sons, Inc., New York, 1958, pp. 291, $9.75.

Dr. David Kritchevsky of the University of Pennsylvania has provided his readers with a well integrated book dealing with both the laboratory and clinical aspects of the "cholesterol problem." Unlike most volumes on cholesterol, this one is not a symposium containing chapters by several contributors, but a unified work written entirely by the author.

Since Dr. Kritchevsky is a biochemist, it follows that five of the seven chapters deal with the chemical and physiological aspects of the subject. These chapters are concerned with (1) Chemistry, (2) Biosynthesis, (3) Absorption and Transport, (4) Metabolism and (5) Analysis of Cholesterol. The author is completely at ease when writing on these phases of the problem. Each chapter is lucidly written and comprehensive in the inclusion of the references available through 1957.

There is no part of the five chapters that could not be read with profit by the clinician interested in this subject, and that on the Metabolism of Cholesterol is essential to a clear understanding of the clinical section of this book. For workers primarily interested in the laboratory aspects, these chapters are worthy additions to the existing literature and contain an excellent bibliography.

The clinical chapters on (1) Cholesterol in

Disease States and (2) The Blood Cholesterol deal primarily with the cholesterol-coronary atherosclerosis relationship, with a brief reference to the possible role of sterol in carcinogenesis.

Despite the fact that Dr. Kritchevsky is not a physician, these two chapters are also well done, with an attempt by the author to present the varying viewpoints of the controversial questions concerning the precise role of cholesterol in atherogenesis, the effect of diet on serum cholesterol and coronary atherosclerosis, and the effectiveness of various cholesterol-lowering agents.

The book closes with an appendix containing a wealth of chemical and physiologic facts about cholesterol, including a list of average blood cholesterol levels of various animals.

As the author states in his preface, "every chapter will be open to criticism from experts in that field," but, taken as a whole, the volume can be recommended from either the clinical or non-clinical standpoint.

LOUIS E. SCHAEFER, M.D.

Handbook of Respiration, edited by Dorothy S. Dittmer and Rudolph M. Grebe. W. B. Saunders Co., Philadelphia, 1958, pp. 403, $7.50.

It has been said that medicine began to make its greatest strides when quantitation of biological data appeared. The evolution of improved physiological and biological technics has led to a vast expansion of our knowledge of biological processes. Unfortunately, this expansion has outstripped our ability to learn, much less retain a precise knowledge of the quantitative data gathered in the past years.

Great credit is due to the editors of the "Handbook of Respiration" and to their many contributors and reviewers. This work represents the most complete compilation to date of respiratory data on man and lower animals, including invertebrates. The general sections covered include basic physical and chemical data, basic respiratory anatomy, lung volumes and pulmonary function, blood respiratory characteristics, erythrocytes and respiratory pigments, mechanics of breathing and eight other sections. Within each of these subdivisions the most detailed data relative to age, sex differences, effects of exercise, drugs and of other factors, such as radiation, are all considered.

The work itself consists of 169 tables with appended references in which even the most demanding investigator will find whatever he seeks of normal, physiologic and pathologic respiratory values. It is well printed, clearly outlined and has a good index. There is also an appendix of valuable nomograms and respiratory equations.

This book is indispensable for all medical libraries, for all laboratories or other facilities interested in cardiopulmonary function, and for all physicians having an interest in the biology of man. The only shortcoming is an attractive but not very durable soft cover binding. It threatens not to survive the frequent use which will be made of this superb handbook.

M. BADER, M.D.
R. BADER, M.D.

Intra Vascular Catheterization, edited by Henry A. Zimmerman. Charles C Thomas, Springfield, Ill., 1959, pp. 782, $16.75.

The technics involved in the rapidly expanding field of intravascular catheterization are ably presented by several outstanding investigators in this useful and timely book, edited by Dr. Zimmerman.

Because of the inclusion of precise technical details, as well as more advanced physiologic considerations, this volume should be of value both to individuals attempting to establish catheterization laboratories as well as to those who are experienced investigators. As a compendium of existing knowledge in the field, with an excellent bibliography, it also should provide a valuable reference work for students of medicine.

The book includes chapters on right and left heart catheterization, as well as catheterization of the hepatic, renal and cerebral circulations. Newer technics in the application of dye dilution curves to the localization of shunts are superbly presented by pioneer investigators in this field—the Mayo Clinic group. Intracardiac electrocardiography and selective angiocardiography are among the other topics which are effectively presented.

Any volume composed of the contributions of several authors can be expected to be somewhat uneven and repetitious and this volume has not escaped. The faults to be found, however, do not seriously detract from its value.

Fisher's chapter on left heart catheterization is well presented, but alternative methods to the posterior puncture technic, such as the

bronchoscopic approach (which may be associated with less mortality) or the anterior approach to the left ventricle (of value in children) are given scant attention.

An indication of rapidity of developments in clinical investigative technics in modern cardiology is the lack of attention given the recent use of radioactive substances, such as Kr^{85} or I^{131} in shunt localization, even in this recently published volume. The technic of aortic injections of dye with sampling at the femoral artery in localizing left-to-right shunts originating in the aorta is also omitted.

Somewhat superfluous in a volume concerning intravascular catheterization are sections on the treatment of chronic pulmonary disease as well as discussions of alterations in the cerebral circulation in various disease states.

The criticisms, however, should be considered as relatively minor. This volume satisfies an increasing need to have precise information about specialized technics easily available. It is, at present, the best in its field and deserves wide circulation. LESLIE A. KUHN, M.D.

Physiology of Cardiac Surgery, by Frank Gollan. Charles C Thomas, Springfield, Ill., 1959, pp. 77, $4.50.

This small volume, consisting of material presented in a recent lecture by the author, is a concise and informative presentation of some of the major physiologic problems facing the cardiac surgeon.

Dr. Gollan devotes a chapter each to hypothermia, extracorporeal circulation and the combination of extracorporeal circulation with hypothermia produced by extracorporeal cooling. These are not attempts to completely review the rapidly expanding literature in these fields, but are critical analyses of their more important aspects. No one is more qualified to do this than the author, a productive and imaginative investigator whose contributions have been many. The lucid presentation of the known facts combined with a nice sense of history and appropriate perspective as to the role of the modern physiologic investigator combine to make this volume not only valuable for its information, but also a delight to read.

There are few criticisms of major degree that can be directed against the volume. It is unfortunate that much of the knowledge in these fields is fragmentary, leaving wide gaps that it is hoped will be filled in the future. The description of pressure-flow relationships during extracorporeal circulation is somewhat confusing in that it is claimed that there is increased vascular resistance. Yet it is also mentioned that even if the extracorporeal blood flow approximates the previous cardiac output of the patient, aortic pressure is lower during perfusion. These facts suggest vasodilatation rather than vasoconstriction.

As the author states in his preface "the two most important research tools are still the cerebral hemispheres of the investigator." This should be borne in mind in our modern era of gadgeteering. The physiologic considerations involved in the increasingly applied technics of extracorporeal circulation and hypothermia should be intimately known by the surgeon, cardiologist and anesthesiologist. This volume is extremely helpful in achieving that end. LESLIE A. KUHN, M.D.

Differential Diagnosis of Internal Diseases, by R. Hegglin. Georg Thieme Verlag, Stuttgart, 1958, pp. 819, $18.95.

This book has now appeared in its sixth edition, seven years after its first appearance. It appears destined to become a classic in its field.

The author is a representative of that vanishing creed of professors of medicine who are ambitious, industrious and vigorous enough to attempt to remain masters in the wide field of internal medicine, in the tradition of the best European medical schools. He approaches the problem of diagnosis from the point of view of the conscientious, well trained practitioner faced with a symptom or group of symptoms in a patient and realizing his responsibility for arriving at the best possible diagnosis with the least possible delay.

The author fulfills this task in a masterly way. In some sections the presentation of the differential diagnosis is broad and very readable, in other sections the author limits himself to a diagrammatic listing of the salient features. He devotes a relatively large space to more uncommon syndromes and disease entities; in the opinion of this reviewer he rightly does so since a textbook of this kind is more likely to be consulted when unusual and puzzling situations are encountered.

For the cardiologist it might be mentioned that the chapters on dyspnea, cardiac arrhythmias, electrocardiographic findings, cyano-

sis and chest pain cover all the cardiovascular diagnostic problems of practical importance. The quality and the selection of illustrations and roentgenograms are excellent.

In the introduction, Dr. Hegglin enumerates factors, compiled by the French clinician Fiessinger, which notoriously lead to errors in diagnosis. They are (1) ignorance, (2) inadequate examination because of bad habits, poor facilities, wrong technic or rushing, (3) errors in judgment because of lack of constructive thinking, stubbornness, preconceived ideas, conceit and vanity, illogical inferences, timid character, tendency to make "interesting" diagnoses and other peculiarities of the examiner, such as habitual pessimism or boundless optimism. The author appears to be singularly free of these stigmas.

It is to be hoped that an English translation will make this book accessible to English-speaking readers.

ALFRED VOGL, M.D.

The Management of Emergencies in Thoracic Surgery, by John Borrie. Appleton-Century-Crofts, Inc., New York, 1958, pp. 340, $10.00.

Borrie's "The Management of Emergencies in Thoracic Surgery" represents a new variation in medical writing. Not only has Borrie attempted (and rather adequately) to detail the prompt and effective treatment of what are ordinarily considered emergencies in thoracic surgery but also he has laid out in elementary form the principles which make for success in non-emergency types of thoracic surgical interventions. Thus, he has presented in simple form the essence of the disturbances of physiology, the diagnostic measures and the principles of surgical management in such conditions as chronic empyema, bronchiectasis and certain esophageal lesions, some of which obviously do not represent acute emergencies.

While the coverage of the subject matter, therefore, is much more comprehensive than is suggested by the title, there is much need for a simple and practical presentation of these problems of which every mature thoracic surgeon is cognizant but with regard to which our residents in training may find themselves, in some respects, deficient. Such information is extremely valuable to the general surgeon who must occasionally manage a thoracic problem.

While there may be individual differences of opinion with regard to the treatment of certain aspects of thoracic disease, the opinions presented in this text are basically sound, and whenever a subject is controversial, Mr. Borrie lucidly expresses the reasons for his specific recommendations.

The book is well illustrated throughout, resulting in clarification of certain aspects of the presented material which might otherwise be somewhat confusing. Altogether I feel that this is a most commendable effort and a valuable addition to our surgical literature.

CHARLES P. BAILEY, M.D.

The Practical Evaluation of Surgical Heart Disease, written and compiled by Robert G. Trout, edited by Robert P. Glover. McGraw-Hill Book Company, Inc., New York, 1959, pp. 132, $10.00.

This volume covers the more common congenital and acquired heart diseases which are presently amenable to operative surgery. It consists of four parts: Part 1 includes very brief basic considerations of the physiologic, radiographic and electrocardiographic observations; Part 2 covers the clinical and laboratory findings in the various diseased states, including the indications for surgery and its results. The subjects covered are patent ductus arteriosus, coarctation of the aorta, vascular rings, pulmonary stenosis, interatrial and interventricular septal defects, tetralogy of Fallot, transposition of the great vessels, mitral stenosis and insufficiency, aortic stenosis and insufficiency and coronary artery insufficiency; Part 3 covers the diagnostic technics of cardiac catheterization and angiocardiography; and Part 4 includes an up-to-date bibliography of value.

An interesting feature in the book is a recording of the heart sounds and murmurs in the various diseased states of the heart covered in the text. This was prepared by Dr. J. Scott Butterworth.

The material is briefly but adequately covered in a systematized and easily readable manner, and the illustrations were carefully chosen and are excellent. One may disagree with the interpretation of some of the electrocardiograms. Particularly serious errors are found in the two electrocardiograms on page 101 where an anterior left ventricular wall infarction is labeled "acute posterior myocardial infarction" and a posterior left ventricular wall infarction is labeled "acute anterior myocardial infarction." In the former tracing, leads III and aVF are

placed upside down. These errors are evidently due to carelessness on the part of the printers and of the technician who prepared the illustrations. With these exceptions, which are minor in nature in view of the abundance of material presented, this reviewer considers this book one of the best of its kind and up-to-date in its presentation. It is highly recommended to any practitioner in medicine and surgery who is interested in cardiology.

LOUIS H. SIGLER, M.D.

Long-Term Illness; Management of the Chronically Ill Patient, edited by Michael G. Wohl. W. B. Saunders Co., Philadelphia, 1959, pp. 748, $17.00.

As stated in the preface, the aim of this book is to present in one volume a comprehensive survey of the management of the patient with prolonged illness. The book is designed primarily for the practicing physician who maintains an interest in the total care of the patient with prolonged illness, for the medical student and for the rehabilitation worker. The reviewer believes the book carries out these objectives very well. It is simply written, easy to read and up-to-date.

The book is divided into two sections. The first part discusses the general principles of hospital and home care, rehabilitation, psychologic problems and nursing procedures in the chronically ill, and multiphasic screening for long term illness. The second part deals with treatment of specific diseases. Special emphasis is placed on therapeutic procedures which are of proved value in the experience of its authors.

The cardiologist will not find diseases of the cardiovascular system completely covered. Chapter 7, "Cardiovascular Diseases," includes only the treatment of chronic cardiovascular disease caused by coronary atherosclerosis and hypertension which account for over 90 per cent of all deaths from heart disease. However, many chapters integrate cardiovascular data pertinent to the subject under discussion.

Elimination of repetitious statements on the importance of chronic disease and its increased incidence in an older population would shorten the first section considerably, especially since Dr. Chauncey Leake alludes to these well known facts in a provocative historical prolegomenon. Asking "Who are the chronically ill?," he answers succinctly "If we live to be sixty, all of us will have some disorder or other of the circulation, of the bowels, of the bones and joints, or of the nervous system. There are about 5,500,000 people quite disabled by chronic disease or impairment in the United States and at least four times as many suffer from minor or temporary chronic or crippling conditions."

This book is well worth reading and owning.

RAYMOND HARRIS, M.D.

Atlas Intracardialer Druckkurven (Atlas of Intracardiac Pressure Curves), by O. Bayer and H. H. Wolter. Georg Thieme Verlag, Stuttgart, 1959, pp. 185, DM 68.

Five years ago the same authors, in collaboration with Loogen, published an excellent monograph on cardiac catheterization in congenital and acquired heart disease. The present book limits itself to description and interpretation of intracardiac pressure curves. The text and legends of the very numerous illustrations are presented in three languages; German, English and Spanish, thereby broadening the availability of the information considerably, although the reviewer agrees with Dr. Cournand that the omission of a French translation is regrettable and should be corrected in a future edition.

Unlike their previous monograph, referred to before, the text is limited and concise but still very informative. The theory and technic of pressure recording is well documented with diagrams and specially selected pressure curves. Interpretation of individual curve contours and their physiologic origin is clearly discussed, including artifacts as a possible source of misinterpretation. There are fifty-five illustrations and forty-two plates in the atlas section, with three to six individual curves to each plate. The technical quality of the curves and their correlation with electro- and phonocardiograms provide excellent teaching material. The coverage of clinical conditions seems almost complete.

The printing of text and illustrations is excellent. The book is highly recommended to cardiologists, cardiac physiologists, pediatricians, internists and particularly to all students of cardiac dynamics. A. GRISHMAN, M.D.

College News

Election of Officers for 1959–60

The following officers were elected at the Eighth Annual Meeting of the American College of Cardiology in Philadelphia on May 27, 1959.

PRESIDENT-ELECT
Louis F. Bishop, Jr., *New York*

FIRST VICE-PRESIDENT
Claude S. Beck, *Cleveland*

SECOND VICE-PRESIDENT
Richard J. Bing, *St. Louis*

THIRD VICE-PRESIDENT
David Scherf, *New York*

SECRETARY
E. Grey Dimond, *Kansas City, Kan.*

ASSISTANT SECRETARY
Irving Brotman, *Washington, D. C.*

TREASURER
William L. Wheeler, Jr., *New York*

ASSISTANT TREASURER
Jerome Noble, *New York*

TRUSTEES FOR FIVE YEARS
Clarence M. Agress, *Beverly Hills*
Richard J. Bing, *St. Louis*
J. Maxwell Chamberlain, *New York*
Gerrit W. H. Schepers, *Newark, Del.*

Osler A. Abbott, *Atlanta, Ga.*, was installed as the new President of the College to succeed George W. Calver, *Washington, D. C.*

Honorary Fellows

Certificates of Honorary Fellowship were conferred on the following distinguished cardiologists at the Eighth Annual Convocation of the College in Philadelphia on May 27, 1959:

Francis L. Chamberlain, *San Francisco*
Irvine H. Page, *Cleveland*
Paul Wood, *London*

The Groedel Medal was awarded to Paul Klemperer, New York, who delivered the Groedel Memorial Lecture on Humanities in Medicine.

Eighth Interim Meeting

The Eighth Interim Meeting of the College will be held in Philadelphia on October 23–25, 1959. This year for the first time the Interim Meeting will be held concurrently with the 32nd Annual Scientific Sessions of the American Heart Association. The College will collaborate in the Scientific Sessions by presenting a symposium jointly with the Council on Clinical Cardiology on Sunday afternoon, October 25. The subjects of the symposium will be "Cardiac Resuscitation" and "Assisted Circulation."

In addition, the College will expand its usual popular Fireside Conferences in which both College and Heart Association members will participate. These will be conducted Friday evening, October 23, following the College dinner. College headquarters will be at the Benjamin Franklin Hotel.

Announcements

Second Annual Symposium on Cinefluorography

The Second Annual Symposium on Cinefluorography sponsored by The Department of Radiology, University of Rochester School of Medicine and Dentistry, will be held on November 13 and 14, 1959, at the University of Rochester Medical Center. The program will emphasize cardiovascular studies. Papers (20 minutes each) are invited on cinefluorographic studies, particularly of the cardiovascular apparatus. Please address papers or inquiries to G. H. Ramsey, M.D., Strong Memorial Hospital, Rochester 20, N. Y.

Sixth Inter-American Congress of Cardiology

The Sixth Inter-American Congress of Cardiology, under the auspices of the Inter-American and Brazilian Societies of Cardiology, will be held from August 14 through 20, 1960, in Rio de Janeiro, Brazil. Prof. E. Magalhães Gomes is President of the Congress.

All correspondence pertaining to this Congress should be addressed to the Secretary, H. Alquéres, Caixa Postal 1594, Rio de Janeiro, Brazil.